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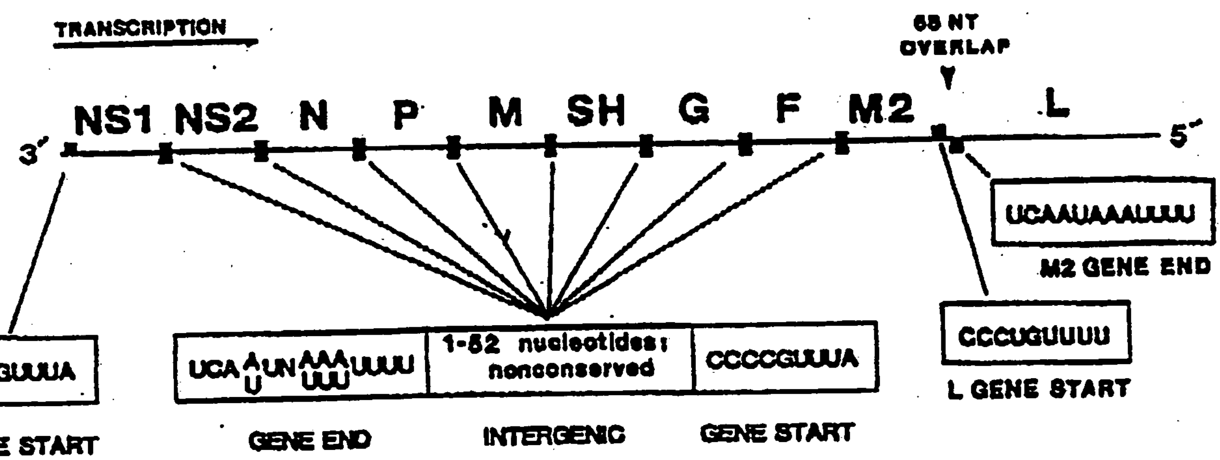

(57) Abstract

The present invention relates to genes derived from bovine respiratory syncytial virus (BRSV). The invention also relates to vectors produced with the genes, expression systems for the genes, as well as diagnostic probes comprising the genes, recombinant proteins and vaccines. The recombinant nucleocapsid protein is particularly useful for diagnostic testing for early detection of a BRSV infection.

BOVINE RESPIRATORY SYNCYTIAL VIRUS GENES

RELATED APPLICATIONS

This is a continuation-in-part of United States patent application Serial No. 07/608,937, filed November 5, 1990.

BACKGROUND OF THE INVENTION

Bovine Respiratory Syncytial Virus (BRSV) is an RNA virus which is recognized as an important cause of lower respiratory disease of cattle in Asia, Europe and the United States. In cattle, BRSV infection is more significantly associated with respiratory disease than any other virus. Furthermore, the highest incidence of severe BRSV disease in cattle is between 2 and 4.5 months of age. About 70 percent of cattle have been infected by BRSV by 9 months of age.

The characteristics of BRSV infection include extensive damage to the mucuous membranes, leaving the respiratory tract susceptible to dust, debris and secondary infectious agents. BRSV infection also causes a condition which resembles systemic anaphylaxis or hypersensitivity. Outbreaks of BRSV infection usually last about 10 to 14 days, and are characterized by high mortality.

However, BRSV is not easily grown, is closely associated with the cell membrane and is inherently unstable (Stott and Taylor, Arch. Virology 84, 1 (1985)). Therefore, purification of the virus by biophysical techniques is extremely difficult.

Antibodies to BRSV were first found in cattle sera in 1968, and in 1970, the virus was isolated. BRSV, human respiratory syncytial virus (HRSV) and pneumonia

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virus of mice comprise the g nus Pneumovirus which is within the family Paramyxoviridae.

Viruses of this family have enveloped pleomorphic virions which contain helical, elongated nucleocapsids. The genome is linear, single-stranded RNA which replicates in the cytoplasm.

Morphologically, the BRSV virion appears as round or pleomorphic forms which measure about 80 to 500 mm across, or as filamentous forms up to several um in length. The outer membrane of the virion is studded with projections about 12 mm long, each of which is about 10 mm apart.

Purified virions contain a unique species of single-stranded RNA of which at least 93 percent is negative sense. Discrepancies regarding the size and number of polypeptides in the virion are due, in part, to differences between virus strains (Stott and Taylor, supra).

Two small polypeptides have been detected. The smaller polypeptide has a molecular weight between about 10,000 and 13,000 daltons, and the larger polypeptide has a molecular weight between about 19,000 and 25,000 daltons. The large polypeptide is a non-glycosylated protein. Neither of the small polypeptides has any known functions (Stott and Taylor, supra).

A larger protein, the M protein (about 27,000 to 28,000 daltons) is believed to be the membrane protein. The M protein has 256 amino acids, and is relatively basic with two hydrophobic regions in the C-terminal third of the protein.

The P protein is a phosphorylated protein with a molecular weight of about 32,000 to 38,000 daltons. This protein is associated with the nucleocapsid.

However, the nucleocapsids isolated from purified BRSV contain primarily NP protein in association with

RNA. The NP protein has a molecular weight of between about 40,000 and 44,000 daltons, and has 467 amino acids, most of which are basic amino acids.

Two glycoproteins which are believed to be located on the surface of the virion are the F protein and G protein. The F protein has a molecular weight of between about 66,000 and 68,000 daltons, and the G protein has a molecular weight of between about 79,000 and 90,000 daltons. These two proteins have a rod-shaped morphology, suggesting that they may be the studded projections of the virion.

The F protein is comprised of two smaller glycoproteins linked by disulfide bonds. One of the smaller glycoprotein has a molecular weight between about 43,000 and 56,000 daltons and the other smaller glycoprotein has a molecular weight between about 19,000 and 22,000 daltons. The F protein has been shown to be the fusion protein by the inhibition of cell fusion by a monoclonal antibody to the F protein.

The G protein is believed to be the attachment protein of the virion. Monoclonal antibodies to either the F protein or the G protein neutralize infectivity of the virus.

There is little known about the largest polypeptide, the L protein. This protein has a molecular weight of between about 160,000 daltons and 200,000 daltons and is believed to be the RNA polymerase of the virion.

Although BRSV and HRSV differ in plaque reduction tests using bovine sera, cattle have been reported to be equally protected from BRSV infection by either BRSV or HRSV antibodies. Any differences detected by neutralization are believed to reflect changes in the epitopes on either the F protein or G protein (Stott and Taylor, supra). Furthermore, two monoclonal antibodies to the BRSV fusion protein appear to react

complement fixation and immunofluoresence tests, all strains of respiratory syncytial virus cross-react (Stott and Taylor, supra).

Regarding respiratory syncytial virus vaccines, three different vaccines for HRSV have been tested, but found not to provide acceptable immunization against HRSV infection (Stott and Taylor, supra). Specifically, the three vaccines which have been tested are: 1) an inactivated antigen combined with adjuvant given intramuscularly; 2) live attenuated viruses given intranasally; and 3) live modified virus given intramuscularly.

Furthermore, the intramuscular vaccination of cattle with a live mutant strain of HRSV does not confer immunity to the cattle (Stott and Taylor, supra). However, cattle have been protected against BRSV infection by intramuscular vaccination with glutaraldehyde-fixed, respiratory syncytial virus - infected bovine nasal mucosa cells (Stott and Taylor, supra).

Another experimental attenuated BRSV vaccine has been reported to be successful by Bohlender et al. In the August, 1982 issue of Modern Veterinary Practice at page 613. This vaccine was found to reduce the average morbidity among calves receiving the vaccine by about half.

Although BRSV and HRSV have traditionally been classified in the same genus, Pneumovirus, as stated above, at least one group of researchers have suggested that these two viruses be classified in separate groups of the genus (Lerch et al., J. Virol. 64, 5559 (1990)). A comparison of the amino acid sequences of the G protein of BRSV with the G protein of either subgroup A or B of HRSV showed only a 29 to 30% amin acid identity. Furthermore, antisera to the BRSV G protein, made by using a recombinant vector to

immunize animals, recognized the BRSV G protein but not the HRSV G protein, and vice versa (Lerch et al., supra).

As is evident from the seriousness of BRSV infection, a rapid diagnostic test for this virus, and a vaccine which would prevent such infection are greatly needed. However, there are no rapid diagnostic tests, and the known vaccines have been ineffective and/or difficult to produce. Particularly, live attenuated BRSV vaccines are unstable, and killed vaccines have been found to be unsatisfactory because the inactivation process probably alters immunogenic epitopes on the virion surface.

SUMMARY OF THE INVENTION

Recognizing the severity of BRSV infection, the present invention relates to genes derived from BRSV, vectors produced with the genes and expression systems for the genes. The genes comprise the nucleotide sequences set forth as in the Sequence Listing as SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6; SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14; SEQ ID NO:16, and SEQ ID NO:18. The invention further relates to fragments of these genes.

The invention also encompasses diagnostic probes comprising these genes or fragments thereof. All of the genes or their fragments are useful as diagnostic probes.

The invention further encompasses purified BRSV proteins or fragments thereof. These purified proteins and fragments can be used to detect BRSV antibodies, and can be used as vaccines. The purified proteins which are useful for the detection of BRSV antibodies and as vaccines are proteins set forth in the Sequence Listing as SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ

ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, and SEQ ID NO:19. However, the protein of SEQ ID NO:3 is particularly useful for diagnostic testing for the presence of BRSV antibodies.

A further aspect of the invention are antibodies to the gene products or fragments thereof.

BRIEF DESCRIPTION OF THE FIGURES

The various objects, advantages and novel features of the invention will be more readily appreciated from the following detailed description when read in conjunction with the appended figures in which:

Fig. 1 shows the genetic map of BRSV strain A2;

Fig. 2 shows an SDS-PAGE gel in which [^{3}H] glucosamine labeled antigens were immunoprecipitated with BRSV (strain A51908) antiserum; and

Fig. 3 shows an autoradiograph of the hybridization of ^{32}P-labeled BRSV-N gene probe to the RNA of a variety of bovine respiratory viruses.

DETAILED DESCRIPTION OF THE INVENTION

In order to provide a clear and consistent understanding of the specification and the claims, the following definitions are provided:

Adjacent: A position in a nucleotide sequence immediately 5' or 3' to a defined sequence.

Cell Culture: A proliferating mass of cells which may be in an undifferentiated or differentiated state.

As used herein "cell", "cell line", and "cell cultur " are used interchangeably and all such designations include progeny. Thus "transformants" or "transformed cells" includes the primary subject cell and cultures derived therefrom without regard for the number of tranfers. It is also understood that all progeny may not be precisely identical in DNA content, due to deliberate or inadvertent mutations. Mutant progeny which have the same functionality as sreened for in the originally transformed cell, are included. Where distinct designations are intended. it will be clear from the context.

<u>Coding Sequence</u>: A deoxyribonucleotide sequence which when transcribed and translated results in the formation of a cellular protein, or a ribonucleotide sequence which when translated results in the formation of a cellular protein.

<u>Control Sequences</u>: Refers to DNA sequences necessary for the expression of an operablylinked coding sequence in a particular host organism. The control sequences which are suitable for procaryotes, for example, include a promoter, optionally an operator sequence, a ribosome binding site, and possibly, other as yet poorly understood, sequences. Eucaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

<u>Expression System</u>: Refers to DNA sequences containing a desired coding sequence and control sequences in operable linkage, so that hosts transformed with these sequences are capable of producing the encoded prot ins. In order to effect transformation, the expression system may be included

on a vector; however, the relevant DNA may then also be integrated into the host chromosome.

<u>Gene</u>: A discrete nucleic acid region which is responsible for a discrete cellular product.

<u>Operably Linked</u>: Refers to juxtaposition such that the normal function of the components can be performed. Thus, a coding sequence "operably linked" to control equences refers to a configuratin wherein the coding sequence cn be expressed under the control of these sequences.

<u>Promoter</u>: The 5'- flanking, non-coding sequence adjacent a coding sequence which is involved in the initiation of transcription of the coding sequence.

<u>Substantial Sequence Homology</u>: Donates nucleotide sequences that are substantially functionally equivalent to one another. Nucleotide differences between such sequences having substantial sequence homology will be <u>de minimus</u> in affecting the function of the gene products or an RNA coded for such a sequence.

With the above definitions in mind, the present invention relates to the novel genes and gene fragments derived from BRSV. The entire genome for BRSV strain A 51908 is presented in SEQ ID NO:1. The genes and gene fragments thereof are:

1. the nucleocapsid protein gene (the N gene) (SEQ ID NO:2);

2. the matrix protein gene (the M gene) (SEQ ID NO:4);

3. the phosphoprotein gene (the P gene) (SEQ ID NO:6);

4. the small hydrophobic protein gene (the SH gene) (SEQ ID NO:8);

5. the fusion protein gene (the F gene) (SEQ ID NO:10);

6. the glycoprotein gene (the G gene) (SEQ ID NO:12); and

7. the M2 protein gene (SEQ ID NO:14).

The position of these genes in the BRSV genome is shown in the gene map of Fig. 1.

These genes were derived from two strains of BRSV. The genes designated by SEQ ID NOS. 2, 4, 6, 8, 10, 12 and 14 above were derived from BRSV strain A 51908, which is available from the American Type Culture Collection (ATCC #VR-794). The other strain is strain FS-1, which is available from the National Veterinary Services Laboratory (NVSL) U.S.D.A., Ames, Iowa. Only the P gene and F gene have been isolated and sequenced from BRSV strain FS-1. The P gene of BRSV strain FS-1 is set forth in the Sequence Listing as SEQ ID No:16, and the F gene of this strain is set forth as SEQ ID NO:18.

As has been recognized in HRSV, there are distinct differences between strains, and knowledge of these differences is necessary for the understanding of clinical and epidemiological characteristics, as well as for vaccine development. With the use of polyclonal and monoclonal antibodies, two distinct antigenic subgroups (A&B) of HRSV have been recognized. It has

been found that viruses of both subgroups circulate in nature, and that for a vaccine to be effective, viruses from both the subgroups must be included. Both antigenic and structural differences between subgroups have been described for several HRSV proteins. Distinct differences in the size of the homologous fusion (F) protein cleavage products and phosphoprotein (P) of subgroup A and B viruses have been demonstrated.

In contrast, to HRSV, antigenic and structural comparisons among strains of BRSV have not, until now, been reported. Recently, Lerch _et al._ compared BRSV strain 391-2 with HRSV strain A_2 (Lerch _et al._, _J. Virol._ 63, 833 (1989)). The most striking difference was found in the F_2 fragment. The F_2 fragment of BRSV strain 391-2 had a lower molecular weight than the F_2 fragment of HRSV.

However, the present inventors have compared the polypeptides of four strains of BRSV. Based on the size of the F_2 fragment and P protein the BRSV strains examined could be classified into groups.

Fig. 2 shows the different migration patterns of the F_2 protein of different strains of BRSV. Particularly, lanes 3-6 show four different strains of BRSV. The BRSV strains in lanes 3 and 5 (FS-1 and VC-464, respectively) have a heavier F_2 protein than the BRSV strains in lanes 4 and 6 (A51908 and Md-x, respectively). Furthermore, BRSV strains A51908 and Md-x have an F_2 protein of the same size as that of HRSV (lane 2), whereas the F_2 protein of BRSV strains FS-1 and VC-464 is smaller than that of HRSV.

The difference in the size of the F_2 fragment is significant because the F_2 fragment contains most of the immunogenic and neutralizing epitopes of the most important envelope protein. Therefore, like HRSV, an effective vaccine against BRSV will require

incorporation of genes from viruses of both structural groups.

BRSV strain 391-2 which was used by Lerch _et al._, _supra_, was isolated from an outbreak of respiratory disease in calves in North Carolina. The immunogenic and pathogenic potential, based on the characterization of the F_2 fragment, of this strain has never been reported.

In contrast, strain A 51908 and strain FS-1 of BRSV, used by the present inventors, are the reference strains in the United States. Strain A 51908 has been found to cause respiratory disease and induction of neutralizing and protective antibodies in experimental infections (Mohanty _et al._, _J. Inf. Dis._ _134_, 4095 (1976)). Strain FS-1 is the first isolate of BRSV in the United States, and also has been found to cause respiratory disease in calves (Smith _et al._, _Arch. Viral._ _47_, 237 (1975)).

Molecular cloning of BRSV genes from any strain is very difficult due to a number of attributes characteristic of BRSV replication. Some of these attributes are that: (1) BRSV has a very narrow host range; (2) BRSV yield is very low; (3) BRSV fails to depress host cell protein synthesis; and (4) BRSV is very labile.

Therefore, a number of cell lines and growth conditions were examined before the optimal conditions for maximum virus yield were determined. Madin Darby bovine kidney (MDBK) cells, 3% bovine fetal serum in maintenance medium, fresh virus stocks without freezing and thawing, and harvest at 48 hours after infection were found to be the optimal growth conditions. It was also found that treatment with Actinomycin D at a concentration of 2.5 μg/ml for 4 hours prior to harvesting cells for mRNAs inhibited some host cell mRNA synthesis. However, higher concentrations or long

SDS-PAGE (Cash et al., Virology 82, 369 (1977) and Lerch et al., J. Virol. 63, 833 (1989)).

Comparison of the nucleotide sequence of the BRSV N gene (SEQ ID NO:2) with the published sequence of HRSV N gene revealed an overall homology of 81%. It is interesting to note the high homology with the conserved gene start sequence present in all mRNAs of HRSV.

Additionally, the untranslated region at the 3'-end of the BRSV N gene (SEQ ID NO:2) also shares high homology with the conserved gene end sequence present in all HRSV genes. The consensus HRSV gene start sequence and gene end sequence have also been observed in other BRSV mRNAs. Thus, the presence of these consensus sequences at the start and end of each gene is believed to be a general feature of the respiratory syncytial viruses.

It was also noted that the homology at the 5'-untranslated region (exclusive of the consensus sequence) between the bovine and the human strains is nearly as high as homology between the two strains in the coding region. However, between human strains, the homology of the 5'-noncoding region is significantly higher than the homology of the coding regions.

The predicted amino acid sequence of the BRSV N protein (SEQ ID NO:3) was compared to that of the N protein of HRSV. The N protein of BRSV is identical to that of A2 and 19537 strains of HRSV at 93% of amino acid positions. Most of the amino acid changes correspond to amino acid substitutions. The apparent structure of the N protein does not seem to be affected by the amino acid changes observed. Thus, it appears that the pneumovirus N proteins are highly conserved.

The BRSV N gene (SEQ ID NO:2) is the preferred gene for use as a diagnostic gene probe for the detection of BRSV infection. Of all the genes transcribed in BRSV

infected cells, the N gene is transcribed in the largest quantity. Also, of the three internal protein genes (N, P and M) tested as probes, the N gene probe is the most sensitive. Furthermore, the probe made from the N gene does not hybridize with cognate genes of other bovine respiratory viruses, but did hybridize well with RNAs extracted from different strains of BRSV.

Fig. 3 shows the specificity of the BRSV N gene probe for BRSV strains as opposed to other bovine respiratory viruses. There is clear hybridization of the ^{32}P-labeled BRSV N gene probe to the RNA of RSV strains A51908, AMES (i.e. FS-1), VC-464 and GRSV, whereas there is no hybridization with the RNA of three other bovine respiratory viruses.

The M gene and the P gene are also particularly useful as probes for BRSV RNA. These two genes also exhibit significant homology in various strains of BRSV. The use of nucleotide sequences as probes is fully explained in Keller and Manak, DNA Probes, Stockton Press (1989).

The product of the BRSV N gene (the BRSV N protein) is also very useful as an antigen for the detection of antibodies against BRSV in serum samples. BRSV antibodies are preferably detected by N gene product antigens, because the N gene product (the nucleocapsid protein) is the first protein to appear after BRSV infection (Westenbrink et al., J. Gen. Viral 70, 591 (1989)) and is produced in the largest quantity of all the BRSV proteins produced by virus-infected cells. The BRSV N protein, as well as the other BRSV proteins (the M, P, SH, F, G, and M2 proteins) can be produced through recombinant means or by polymerase chain r action (PCR), as explained further below.

The BRSV proteins can also be used to produce BRSV protein antibodies. In order to produce an anti-BRSV antibody, a rabbit is immunized with either a naturally

periods of treatment with Actinomycin D were toxic to MDBK cells.

As noted above, the fresh virus stocks which were used were BRSV strain A 51908 (ATCC # VR-794) and BRSV strain FS-1 from NVSL, U.S.D.A., Ames, Iowa. Furthermore, the maintenance medium used was Eagle's minimum essential medium with Earle's salts (MEM).

The mRNAs isolated from the BRSV infected cells were used to construct cDNA libraries. However, identification of BRSV-specific clones is very difficult for the following reasons: (1) a very small proportion of the cDNA clones are virus-specific; (2) cDNA clones of HRSV do not hybridize well with mRNAs of BRSV of Northern blot hybridization; and (3) due to the pleomorphic nature of BRSV, it is difficult to purify this virus and use its genomic RNA as a probe to identify virus-specific clones.

However, the present inventors used a number of methods to identify BRSV-specifc clones. Some of these methods are: (1) hybrid arrest and <u>in vitro</u> translation; (2) Northern blot hybridization; and (3) use of cDNA clones of HRSV in different hybridization conditions.

In identifying the BRSV specific clones, viral mRNA was isolated from the BRSV-infected MDBK cells by the guanidine thiocyanate-CsC1 procedure (Chirgwin <u>et al.</u>, <u>Biochemistry</u> <u>18</u>, 5294 (1979)). Poly(A)$^+$-RNA was then purified using oligo (dT) cellulose (Aviv and Leder, <u>Proc. Natl. Acad. Sci. USA</u> <u>69</u>, 1408 (1972)), and double-stranded cDNA was synthesized by the RNase H method of Gubler and Hoffman, <u>Gene</u> <u>25</u>, 264 (1983).

The double-stranded cDNA molecules were then ligated into the EcoRI site of plasmid Bluescript (Stratagene), and the resulting hybrid plasmids were used to transform <u>E.coli</u> JM109 cells using the method described by Cohen <u>et al.</u>, <u>Proc. Natl. Acad. Sci. USA</u>

69, 2110 (1972). Bacterial clones containing recombinant DNA were selected on the basis of their color and resistance to ampicillin. N-specific clones were identified by in vitro translation of mRNA obtained by hybrid-selection of randomly selected cDNA clones (Ricciardi et al., Proc. Natl. Acad. Sci. USA 76, 4927 (1979)).

One clone, designated A60, was selected for further analysis as it contained the largest insert among the N-specific clones. The viral specificity of this clone was further confirmed by Northern blot analysis. The cDNA clone hybridized to poly(A)$^+$-RNA from infected cells, but not to poly(a)$^+$-RNA from uninfected cells.

The nucleotide sequence of the mRNA of the N protein was obtained by sequencing the clone A60 by the dideoxynucleotide chain termination method Sanger et al., Proc. Natl. Acad. Sci. USA 74, 5463 (1977). Clone A60 (1196 bp exclusive of poly(dA)) contained the entire N mRNA sequence lacking only 10 nucleotides of the 5′ end of the mRNA. The nucleotide sequence was confirmed using clone A1032 (1099 bp exclusive of poly(dA)), which expanded from nucleotide 97 to the poly(A) tail of the N mRNA.

The nucleotide sequence of the N mRNA (SEQ ID NO:2) and deduced amino acid sequence of the N protein (SEQ ID NO:3) of BRSV are shown in the Sequence Listing. The nucleotide sequence of the 5′-end untranslated region was obtained by direct sequencing of the N mRNA using a primer complementary to nucleotides 41 to 63.

The BRSV N mRNA contains 1196 nucleotides, excluding the poly(A) tail. The mRNA has a single long open reading frame, extending from nucleotides 16 to 1188. The BRSV N mRNA encodes a polypeptide of 391 amino acids with a calculated molecular weight of 42.6 kD. This value is consistent with the apparent molecular weight of 43 kD determined earlier in

occurring BRSV protein or a recombinant BRSV protein. Alternatively, a monoclonal anti-BRSV antibody is produced using conventional techniques (Meth. Enzymol., Vol. 121, Langone, J.J. and Van Vinakis, H., Ed., Academic Press, Orlando (1986) and Roitt, I., in Essential Immunology, 5th Ed. Blackwell Scientific Publications, Boston, pp. 145-175 (1984)). The anti-BRSV antibody generated is then labeled, e.g., radioactively, fluorescently or with an enzyme such as alkaline phosphatase.

In addition to being the preferred gene for diagnostic purposes, the BRSV N gene is also useful for vaccine production because: 1) the N protein is the most abundant protein in BRSV-infected cells; 2) calves naturally infected with BRSV have high titer antibodies to N protein; and 3) N protein is necessary for cytotoxic T cell activity. The production of a vaccine from the BRSV N gene or any of the other BRSV genes requires the use of the genes or fragments thereof to manufacture recombinant proteins. In order to produce a recombinant protein, the gene (or gene fragment) for the desired protein is operably linked to control sequences to form an expression vector. The expression vector is then used to transform a suitable host, and the transformed host, under suitable conditions, produces a recombinant form of the desired protein.

Recombinant forms of any of the identified BRSV proteins or fragments thereof may be produced in this manner. Particularly, recombinant forms of the BRSV strain A51908 nucleocapsid protein (SEQ ID NO:3), matrix protein (SEQ ID NO:5), phosphoprotein (SEQ ID NO:7), small hydrophobic protein (SEQ ID NO:9), fusion protein (SEQ ID NO:11), glycoprotein (SEQ ID NO:13) and M2 protein (SEQ ID NO:15) are produced in this manner.

Furthermore, recombinant forms of the BRSV proteins or fragments thereof of strain FS-1 can also be

produced in the manner set f rth above. The proteins or fragments thereof of strain FS-1 which have been identified are the P protein (SEQ ID No:17) and the F protein (SEQ ID NO:19).

Each of the steps for production of a recombinant protein can be done in a variety of ways. For example, the desired coding sequences can be obtained by preparing suitable cDNA from cellular messenger and manipulating the cDNA to obtain the complete sequence. Alternatively, genomic fragments may be obtained and used directly in appropriate hosts. The constructions for expression vectors operable in a variety of hosts are made using appropriate replicons and control sequences, as set forth below. Suitable restriction sites can, if not normally available, be added to the ends of the coding sequence so as to provide an excisable gene to insert into these vectors.

The control sequences, expression vectors, and transformation methods are dependent on the type of host cell used to express the gene. Generally, procaryotic, yeast, or mammalian cells are presently useful as hosts. Procaryotic hosts are in general the most efficient and convenient for the production of recombinant proteins. However, eucaryotic cells, and, in particular, mammalian cells are sometimes used for their processing capacity.

The preferred vectors for the BRSV genes are baculovirus and IBR herpes virus. When baculovirus is used as the vector, suitable host cells are insect cells such as Drosophila cells, Trichoplusia ni cells (cell line TN-368) and SF-9 cells, grown maintained under conventional conditions. The preferred host cells are the SF-9 cells. The culturing, maintenance and growth of insect cell lines by Agathos et al., in Annals of the NY Acad of Sciences 589, 372 (1990).

When IBR herpes virus is used as the vector, the host for producing recombinant BRSV protein is a calf.

In addition to the preferred insect host cells, the procaryotes most frequently used are represented by various strains of E. coli. However, other microbial strains may also be used, such as bacilli, for example Bacillus subtilis, various species of Pseudomonas, or other bacerial strains. In such procaryotic systems, plasmid or bacteriophage vectors which contain replication sites and control sequences derived from a species compatible with the host are used. A wide variety of vectors for many procaryotes are known (Sambrook et al., (1989), Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY). Commonly used procaryotic control sequences which are defined herein to include promoters for transcription initiation, optionally with an operator, along with ribosome binding site sequences, include such commonly used promoters as the beta-lactamase (penicillinase) and lactose (lac) promoter systems, the tryptophan (trp) promoter system and the lambda derived PL promoter and N-gene ribosome binding site, which has been made useful as a portable control cassette (U.S. Patent No. 4,711,845). However, any available promoter system compatible with procaryotes can be used (Sambrook et al., supra).

In addition to bacteria, eucaryotic microbes, such yeast, may also be used as hosts. Laboratory strains of Saccharomyces cerevisiae, Baker's yeast, are most used, although a number of other strains are commonly available. Vectors employing the 2 micron origin of replication and, other plasmid vectors suitable for yeast expression are known (Sambrook et al., supra). Control sequenc s for yeast vectors include promoters for the synthesis of glycolytic enzymes. Additional

promoters known in the art include the promoter for 3-phosphoglycerate kinase, and those for other glycolytic enzymes, such as glyceraldehyde-3-phosphase dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, hosphoglycose isomerase, and glucokinase. Other promoters, which have the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, and enzymes responsible for maltose and galactose utilization. (See Sambrook <u>et</u> <u>al</u>., <u>supra</u>).

It is also believed that terminator sequences are desirable at the 3′ end of coding sequences. Such terminators are found in the 3′ untranslated region following the coding sequences in yeast-derived genes. Many of the vectors illustrated contain control sequences derived from the enolase gene containing plasmid peno46 or the LEU2 gene obtained from YEp13, however, any vector containing a yeast compatible promoter, origin or replication and other control sequences is suitable (Sambrook <u>et</u> <u>al</u>., <u>supra</u>).

It is also, possible to express genes encoding polypeptides in eucaryotic host cell cultures derived from multicellular organisms (<u>Meth. Enzymol.</u>, Vol 58, Academic Press, Orlando (1979)). Useful host cell lines include murine myelomas N51, Vero and HeLa cells, and Chinese hamster ovary (CHO) cells. Expression vectors for such cells ordinarily include promoters and control s quences compatible with mammalian cells such as, for example, the commonly used early and later promoters from Simian Virus 40 (SV 40), or other viral

promoters such as those derived from polyoma, adenovirus 2, bovine papilloma virus, or avian sarcoma viruses, or immunoglobulin promoters and heat shock promoters (Sambrook et al., supra). General aspects of mammalian cell host system transformations have been described by Axel (U.S. Patent No. 4,399,216).

It is now also appears that "enhancer" regions are important in optimizing expressin; these are, generally, sequences found upstream of the promoter region. Origins of replication may be obtained, if needed, from viral sources. However, integration into the chromosome is a common mechanism for DNA replication in eucaryotes. Plant cells are also now available as hosts, and control sequences compatible with plant cells such as the nopaline synthase promoter and polyadenylation signal sequences are available (Meth. Enzymol., Vol. 118, Academic Press, Orlando (1979)).

Depending on the host cell used, transformation is done using standard techniques appropriate to such cells. Such techniques include, but are not limited to, calcium treatment employing calcium chloride for procaryotes or other cells which contain substantial cell wall barriers; infection with Agrobacterium tumefaciens for certain plant cells; calcium phosphate precipitation method for mammalian cells without cell walls; and, microprojectile bombardment for many cells including plant cells.

Following production of the recombinant proteins, vaccines may be made by using the protein directly or by attaching a carrier to the recombinant BRSV proteins at the appropriate terminal amino acid. Useful carriers include tetanus toxoid linked to the appropriate amino acid through tyrosine, Lipid A, hepatitis B antigen and/or a microorganism to which the protein may be linked. The preferred carrier is

tetanus toxoid linked to the appropriate terminal amino acid through tyrosine.

A conventional initial dose of such a vaccine would be 50 μg of vaccine in 0.1 ml of Freund's complete adjuvant. Conventionally, two boosts of 50 μg of vaccine in 0.1 ml of Freund's incomplete adjuvant are given at two week intervals after the initial dose.

In addition to the N protein, the envelope proteins are also protective antigens, and the genes of these envelope proteins are also necessary for a recombinant vaccine. These envelope proteins are the F protein and the G protein.

Furthermore, the M protein and the SH protein have properties which suggest that they may also be necessary for an effective vaccine. Although the SH protein was previously thought to be a non-structural protein, the present inventors have shown that the SH protein is a third glycosylated envelope protein, in addition to the F and G proteins. Furthermore, the nucleotide sequence of the SH gene of BRSV (ID SEQ. NO:8) is significantly different from the nucleotide sequence of the SH gene of HRSV .

In order to identify the M gene and the SH gene, cDNA clones were constructed from intracellular poly (A^{+})-RNA isolated from BRSV A51908-infected cells. Recombinant DNA clones containing the M and SH genes were identified by in vitro translation of mRNA obtained by hybrid selection of randomly selected cDNA clones (Ricciardi et al., supra). The nucleotide sequence of the polytranscript mRNA coding for the M and SH proteins was derived from two independent clones, A564 and A22, by the dideoxynucleotide chain termination method (Sanger et al., supra).

The nucleotide sequence coding for the small hydrophobic (SH) protein is 466 nucleotides long (nucleotides 3045 to 3511) (SEQ ID NO:8). The homology

of the coding region, at the nucleotide level, is 45-50% depending on the HRSV strain (Table 1). The gene-start signal was identified as nucleotides 2902 to 2910 by comparison with the HRSV SH mRNA (Collins and Wertz, Virology 141, 283 (1985) and Collins et al., J. Virol. 71 1571 (1990)). The 5' untranslated region, excluding the gene-start signal, is the same length as its counterpart in HRSV and shares 56% sequence identity with HRSV A2 strain but only 41% with HRSV 18537 strain. The 3' untranslated region is 132 nucleotides (compared to 99 in HRSV) with a sequence homology of 50-58%.

The predicted SH proteins from BRSV (A51908 strain) (SEQ ID NO:9) and HRSV (A2 and 18537 strains) can be compared. The predicted BRSV SH protein is 155 amino acids long. It contains a 8-amino acid extension at the carboxyl-end, relative to the HRSV SH protein.

Computer analysis predicts that BRSV SH protein has a central hydrophobic core (amino acids 14 to 41) flanked by two lysine residues (at positions 13 and 43), which are conserved in the HRSV SH proteins (A2 and 18537 strains). This hydrophobic core contains a potential membrane-spanning region (amino acids 20 to 40) similar to the one predicted for the HRSV SH proteins (strains A1 and 18537). There are three potential N-glycosylation sites at positions 2, 3 and 52, but only the one at position 3 is conserved in all three proteins.

The overall homology between the BRSV and HRSV SH proteins is surprisingly low (less than 60%) (Table 1). The amino acid identities are located mainly in the amino-end region (amino acids 1 to 23) (>65%). However, the central hydrophobic core (amino acids 24 to 41) has no more than 34% homology, and the carboxyl-terminal region (amino acids 42 to 65) is highly divergent (>30% homology) (Table 1).

The deduced M protein contains 316 amino acids and has a molecular weight of 28,713 daltons. The BRSV M protein (SEQ ID NO:5) shares an 89% homology with the HRSV M protein , with most of the differences being due to amino acid substitutions.

In relation to the M protein of HRSV, the M protein of BRSV is moderately basic. Computer analysis predicts a single hydrophobic region (residues 188 to 204) that could act as a transmembrane domain in the BRSV M protein. The same region was predicted for the HRSV M protein (Satake and Venkateson, J. Virol. 50, 92(1984)). Comparison of HRSV M gene and BRSV M gene (SEQ ID NO:4) reveals a homology of 80% between coding regions.

The gene-start signal (Collins et al., Proc. Natl. Acad. Sci. USA 83, 4594(1988)) for the BRSV M gene (nucleotides 1 to 10) contains a single nucleotide difference at position 5 compared with the HRSV M gene-start signal, excluding the 5'-terminal nucleotide. The gene-end consensus signal was identified as the sequence from nucleotide 876 to nucleotide 888. The untranslated region at the 3' end, excluding the consensus sequence, is 8 nucleotides shorter in the BRSV mRNA and, as seen in other RSV genes, has a lower homology (51%) with the HRSV counterpart region (Table 1) than the coding region. As in HRSV, there is no untranslated region, other the gene-start sequence, at the 5'-end of the M mRNA of BRSV.

TABLE 1

Summary of the percentage of identity, at both the amino acid and nucleotide level, of the M protein and SH protein from BRSV and HRSV.

M protein

	% Homology BRSV(A51908)/HRSV(A2)
Amino Acid	89
Nucleotide	
- Overall	74
- Coding region	80
- 3′ end *	51

SH protein

	% Homology		
	BRSV/HRSV (A51908) (2)	BRSV/HRSV (A51908) (18537)	HRSV/HRSV (A2) (18537)
Amino acid	44	40	76
- Overall	44	40	76
- N-end	65	70	91
- hydrophobic domain	33	28	84
- ectodomain	30	20	50
Nucleotide			
- Overall	50	45	78
- 5′ end*	56	41	52
- coding region	58	50	74
- 3′ end*	35	39	54

N-end (amino acids 1 to 23)
Hydrophobic domain (amino acids 24 to 41)
Ectodomain (amino acids 42 to 65)
* excluding the gene-start or gene-end consensus signals.

Intergenic region 24 %

The intergenic region between M and SH genes of BRSV is 25 nucleotides long (vs 9 nucleotides in HRSV) and shares only 24% homology with the corresponding region in HRSV, suggesting that this region acts as a mere bridge between genes.

Finally, the polycistronic mRNA studied contains two additional open reading frames. One open reading frame from nucleotides 111 to 266 encodes a protein of 52 amino acids and overlaps with the M gene. A second open reading frame has also been reported for HRSV, encoding a protein of 75 amino acids, overlapping with the M gene (Satake and Venkateson, supra). When the second open reading frames from BRSV and HRSV were compared no homology was found. Another open reading frame in BRSV M-SH polycistronic mRNA was found from nucleotides 1271 to 1423 which encodes a protein of 51 amino acids. No similar protein has been described for HRSV. Since these second open reading frames are not conserved, either at the sequence level or at the relative position in the genome, they probably do not play any role in the virus replication.

Other strains of BRSV can be grown and their genomes cloned in accordance with the description herein. The DNA sequences disclosed herein can be used as probes or to prepare degenerative primers for PCR to isolate the specific individual genes which can be cloned and utilized as described above for these additional strains of BRSV.

The present invention is further illustrated by reference to the following examples. These examples are provided for illustrative purposes, and are in no way intended to limit the scope of the invention.

EXAMPLE 1

Isolation and Sequencing of BRSV Genes

The A51908 strain of BRSV originally isolated in Maryland and available from the American Type Culture Collection (ATCC VR-794), was used in this Example. Madin-Darby bovine kidney (MDBK) cells were grow in Eagle's minimum essential medium with Earle's salts (MEM) containing 6% bovine fetal serum (BFS). The BRSV strain A51908 was then prepared in MDBK cell cultures propagated in MEM containing 3% BFS. The viral mRNA was isolated from the BRSV-infected MDBK cells by the guanidinium thiocyanate-CsCl procedure (Chirgwin et al., supra), followed by two cycles of oligo (DT)-cellulose column chromotography. Double-stranded cDNA was synthesized by the RNase H method of Gubler and Hoffman, supra. The double-stranded cDNA molecules were ligated into the EcoRI site of plasmid Bluescript (Stratagene). The resulting hybrid plasmids were used to transform E. coli JM109 cells using the method described by Cohen et al., supra. Bacterial clones containing recombinant DNA were selected on the basis of their color and resistance to ampicillin.

A total of 1642 ampicillin-resistant white colonies were obtained. All transformants were analyzed for the presence of viral sequences by colony hybridization with (1) ^{32}P-labeled cDNAS made by reverse transcription of mRNAs extracted from BRSV-infection cells; and (2) 5'^{32}P-labeled probe made from base hydrolyzed virion RNA. Over 60% of the total transformants (1016) hybridized strongly with both probes. The identity of these clones was determined by: (1) Northern blot analysis; and (2) in-vitro translation of hyrid selected mRNAS.

A cDNA clone was identified to contain sequences of the major nucleocapsid (N) gene of BRSV. This clone

was used to identify other N gene clones by dot blot hydridization. One clone, designated A60, was selected for further analysis as it contained the largest insert among the N-specific clones. The nucleotide sequence of the mRNA of the N protein was obtained by sequencing the clone A60 by the dideoxynucleotide chain termination method. Clone A60 (1196 bp exclusive of poly(dA)) contained the entire N mRNA sequence lacking only 10 nucleotides of the 5' end of the mRNA. The nucleotide sequence was confirmed using clone A 1032 (1099 bp exclusive of poly (dA)), which expanded from nucleotide 97 to the poly (A) tail of the N mRNA.

The other BRSV genes of strain A51908 (the matrix protein gene, the phosphoprotein gene, the small hydrophobic protein gene, the fusion protein gene, the glycoprotein gene and the M2 protein gene) were isolated and sequenced using the same techniques. Furthermore, the phosphoprotein gene and the fusion protein gene of BRSV strain FS-1 were also isolated and sequenced in the same manner. The sequences of the BRSV genes are set forth in the Sequence Listing as follows:

<u>Strain A51908</u>

SEQ ID NO:2	nucleocapsid protein (N) gene
SEQ ID NO:4	matrix protein (M) gene
SEQ ID NO:6	phosphoprotein (P) gene
SEQ ID NO:8	small hydrophobic (SH) protein gene
SEQ ID NO:10	fusion protein (F) gene
SEQ ID NO:12	glycoprotein (G) gene
SEQ ID NO:14	M2 protein (M2) gene

<u>Strain FS-1</u>

SEQ ID NO:16	phosphoprotein (P)
SEQ ID NO:18	fusion protein (F) gene

EXAMPLE 2

Production of BRSV Genes With The Polymerase Chain Reaction

Two fragments of the BRSV N gene isolated in Example 1 are used as primers in the polymerase chain reaction (PCR) (U.S. Patent Nos. 4,683,195 and 4,683,202, both of which are incorporated herein by reference). A DNA polymerase from Thermus aquaticus (U.S. Patent No. 4,889,818, incorporated herein by reference) is used in an amount of 1.25 units as the enzyme to catalyze the PCR.

In addition to the polymerase, 50 pmol of each primer, 10 copies of the BRSV genome, 200 μM of each dNTP, 2 mM $MgCl_2$, 10 mM Tris-HCl (pH 8.3), and 50 mM KCl are placed in a Perkin-Elmer Cetus Instruments Thermal Cycler. Thirty cycles of 96°C for 15 seconds, 50°C for 30 seconds and 75°C for 30 seconds are run. The BRSV N gene is then recovered using conventional techniques.

The other BRSV genes can also be produced using the above procedure.

EXAMPLE 3

Isolation of BRSV Proteins

The BRSV N gene isolated in Example 1 or produced in Example 2 is inserted into baculovirus (Autographa california Nuclear Polyhedrosis Vrisu (AcNPV) (Voil et al., J. Invertebrate Pathol. 22, 231 (1971)) using conventional techniques to form an expression vector. The expression vector is then used to infect Spodoptera frugiperda (SF-9) cells.

The SF-9 cells are maintained in a serum-free/protein-free medium developed by Maiorella et al., Bio/Technology 6, 1406 (1988). The serum-free/

protein-free medium is composed of IPL/41 medium (JR Scientific, Woodland, CA) supplemented with tryptose phosphate broth (Oxoid USA, Columbia, MD), fetal bovine serum (Gibco, Grand Island, NY), and pluronic polyol F68 (BASF Wyandotte, Porsippamy, NJ).

After infection with the baculovirus expression vector, the SF-9 cells are grown in a medium composed of IPL/41 medium supplemented with cod liver oil polyunsaturated fatty acid methyl esters, cholesterol, alpha-tocopherol acetate, Tween 80 and diluted Yestolate (Difco). The cells are grown in spinner flasks, stirred at 75-100 rpm, at 27°C with an air atmosphere.

Approximately 4 to 5 days post-infection, the BRSV N protein titre peaks as cell lysis begins. SDS-PAGE analysis is then used to identify and isolate the recombinant BRSV N protein. The other BRSV genes from Example 1 may be used in the same procedure described above to isolate and identify their respective recombinant proteins.

While the invention has been described in connectin with specific embodiments thereof, it is understood that the invention is capable of further modifications. This disclosure is inteneded in an illustrative rather than in a limiting sense, as it is contemplated that modifications will readily occur to those skilled in the art, within the spirit of the invention and the scope of the appended claims.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Samal, Siba K

(ii) TITLE OF INVENTION: Bovine Respiratory Syncytial Virus Genes

(iii) NUMBER OF SEQUENCES: 19

(iv) CORRESPONDENCE ADDRESS:
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(C) CITY: Washington
(D) STATE: DC
(E) COUNTRY: USA
(F) ZIP: 20005

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: WO
(B) FILING DATE: 04-NOV-1991
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: US 07/608,937
(B) FILING DATE: 05-NOV-1990

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Highet, David W
(B) REGISTRATION NUMBER: 30,265
(C) REFERENCE/DOCKET NUMBER: 20509-96711

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 202-962-4854
(B) TELEFAX: 202-962-8300

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7323 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 1..1200
(D) OTHER INFORMATION: /label= N gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 1204..2068
(D) OTHER INFORMATION: /label= P gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 2071..3019
(D) OTHER INFORMATION: /label= M gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 3045..3511
(D) OTHER INFORMATION: /label= SH gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 3549..4388
(D) OTHER INFORMATION: /label= G gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 4416..6309
(D) OTHER INFORMATION: /label= F gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 6363..7323
(D) OTHER INFORMATION: /label= M2 gene

(ix) FEATURE:
(A) NAME/KEY: misc_RNA
(B) LOCATION: 7256..7323
(D) OTHER INFORMATION: /label= 3' end L gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GGGGCAAATA CAAAAATGGC TCTTAGCAAG GTCAAACTAA ATGACACTTT CAACAAGGAT 60

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CCCAATTATG ATGTACAAAA ACATCTCAAT AAGTTGTGTG GTATGCTACT AATAACAGAA 180

GATGCCAATC ATAAATTTAC AGGATTGATA GGTATATTAT ATGCTATGTC CCGATTGGGG 240

AGAGAAGATA CCCTTAAAAT ACTCAAAGAT GCAGGCTACC AAGTAAGGGC CAATGGGGTT 300
GATGTGATAA CACATCGACA GGATGTGAAT GGAAAAGAAA TGAAATTTGA AGTGCTAACA 360
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AGATCAGGCC TCACTGCAGT CATTAGGAGA GCCAACAATG TACTAAGGAA TGAAATGAAA 600
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GGAGAAGCTG GTTTTTATCA CATATTGAAC AACCCTAAAG CATCACTGTT ATCCTTAACA 960
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CAATGGCCAG GCTTAGGGAT GAAGAGAGTG AAAAGATGAC AAAAGATACA TCAGATGAAG 1860
TAAAATTAAC CCCTACCTCA GAGAAACTGA ACATGGTATT AGAAGATGAA AGTAGTGACA 1920

ATGATCTATC ACTTGAAGAT TTCTGAACAG CAACCAGCAC ACCAACCAAC AGATTGGTCA 1980
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GCCATCACTA ATGCCAAAAT TATACCTTAT GCTGGGTTGG TGTTAGTTAT CACTGTAACT 2700
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CCAAACCAAC CACCCAACAA ACACAACAGC CCCAAAACCA CACCCCACTA CTTCCCACAG 3840
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AGTAGAGCAA AAAGAGGGAT ACCAGAGTCG ATACATTATA CAAGAAACTC TACAAAAAAG 4800
TTTTATGGAC TAATGGGCAA AAAGAGAAAA AGGAGATTTT TAGGATTCTT GCTAGGTATT 4860
GGATCTGCTA TTGCAAGTGG TGTAGCAGTG TCCAAAGTAC TACACTTGGA GGGAGAGGTG 4920
AACAAAATTA AAAATGCACT GCTATCCACA AATAAAGCAG TGGTTAGTCT GTCCAATGGA 4980
GTTAGTGTCC TTACTAGCAA AGTACTTGAT CTAAAGAACT ATATAGACAA AGAGCTTCTA 5040
CCTAAAGTTA ACAATCATGA TTGTAGGATA TCCAACATAG CAACTGTGAT AGAATTCCAA 5100
CAAAAAAACA ATAGATTGTT GGAAATTGCT AGGGAATTTA GTGTAAATGC TGGTATTACC 5160
ACACCCCTCA GTACATACAT GTTAACCAAT AGTGAGTTAC TATCAATAAT TAATGATATG 5220
CCTATAACGA ATGACCAAAA AAAGCTAATG TCAGTATGTC AAATAGTCAG GCAACAGAGT 5280

TATTCCATCA TGTCAGTGTT AAGAGAGGTC ATAGCTTATG TTGTACAATT GCCTCTTTAT 5340

GGAGTTATAG ACACCCCCTG TTGGAAACTA CACACCTCTC CATTATGCAC CACTGATAAT 5400

AAAGAAGGGT CAAACATCTG CTTAACTAGG ACAGATCGTG GGTGGTATTG TGATAATGCA 5460

GGCTCTGTGT CTTTTTTCCC ACAAGCAGAG ACGTGTAAGG TACAATCAAA CAGAGTGTTC 5520

TGTGACACAA TGAACAGTTT AACTTTGCCT ACTGATGTTA ACTTATGCAA CACTGACATA 5580

TTCAATTCAA AGTATGATTG TAAAATAATG ACATCTAAAA CTGACATAAG TAGCTCTGTG 5640

ATAACTTCAA TAGGAGCTAT TGTATCATGC TATGGGAAGA CAAAATGTAC AGCCTCTAAT 5700

AAAAATCGTG GAATCATAAA GACTTTTTCC AATGGGTGTG ATTATGTATC AAACAAAGGA 5760

GTTGATACTG TATCAGTTGG TAACACACTA TATTATGTAA ATAAACTAGA GGGGAAAGCA 5820

CTCTATATAA AGGGTGAACC AATTATTAAT TACTATAATC CACTAGTATT TCCTTCTGAT 5880

GAGTTTGATG CATCAATTGC TCAAGTAAAC GCAAAAATAA ACCAAAGCCT GGCTTTCATA 5940

CGTCGATCTG ATGAGTTACT TCACAGTGTA GATGTAGGAA AATCCACCAC AAATGTAGTA 6000

ATTACTACTA TTATCATAGT GATAGTTGTA GTGATATTAA TGTTAATAAC TGTGGGATTA 6060

CTGTTTTACT GTAAGACCAG GAGTACACCT ATCATGTTAG GGAAGGATCA GCTTAGTAGT 6120

ATCAACAATC TTTCCTTTAG TAAATGAAAT GCATAATGTT TACAATCTTA ACCTCAGAAT 6180

CATAAATGTG ATGAGCCAAA TTTACTGATA CATTCAAAAG TTCCATCTGC CAAGACCTGC 6240

ATCTTTATCA GGTCTGCACA AGCTAACCTT ACATTCTATA CTCAGCTCTA TGTTAATAGT 6300

TATATAAAAG TATTATATTA ATCTCAAGAT CACCTATTTA ATAACCAATC ATTCAAAAAG 6360

ATGGGGCAAA TATGTCACGA AGAAATCCCT GCAAATATGA GATTAGGGGA CATTGCTTAA 6420

ATGGTAAAAA ATGCCATTTT AGTCATAATT ACTTTGAATG GCCTCCACAT GCTTTATTAG 6480

TGAGGCAAAA TTTTATGCTA AATAAGATAT TAAAATCTAT GGACAGGAAC AACGATACCC 6540

TGTCAGAAAT AAGTGGTGCT GCAGAATTAG ATAGAACAGA AGAATATGCA TTGGGTGTGA 6600

TAGGAGTTTT GGAAAGTTAC TTAAGCTCTA TCAATAATAT AACAAAACAA TCAGCCTGTG 6660

TTGCTATGAG TAAACTATTA GCCGAGATTA ACAATGATGA CATCAAGAGA TTAAGGAACA 6720

AGGAAGTGCC AACATCACCC AAGATAAGAA TATATAACAC AGTTATATCA TATATTGATA 6780

GCAACAAGAG AAACACAAAA CAAACTATAC ATTTGCTTAA GAGATTGCCT GCAGACGTGC 6840

TTAAAAAGAC CATCAAGAAC ACAATAGATA TTCACAACGA AATAAATGGT AATAACCAAG 6900

GTGACATAAA TGTTGATGAA CAAAATGAAT AACTCCAACA TTATTATTTT CCCAGAAAAA 6960

```
TACCCCTGTA GCATATCCTC TTTGCTAATT AAGGATGAAA ATGATGTTTT TGTACTAAGT   7020

CATCAGAATG TTCTTGACTG CTTACAGTTT CAATATCCAT ATAATATGTA TTCTCAAAAT   7080

CATATGCTTG ATGATATCTA TTGGACATCA CAGGAGCTGA TTGAGGATGT ACTTAAGATT   7140

CTTCATCTTT CTGGCATATC CATAAATAAG TATGTGATAT ATGTTTTAGT GCTATAGTAT   7200

ATAAGTCACT CAACTATTGA TCAACAGCCA CTTCTTCATA GCTAGCAATA TATAAGGACA   7260

AAATGGATAC ACTCATTCAT GAGAACTCAA CTAATGTTTA CTTAACAGAT AGTTATTTAA   7320

AAA                                                                 7323
```

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1197 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
 (A) ORGANISM: Bovine respiratory syncytial virus
 (B) STRAIN: A 51908

(ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 16..1188
 (D) OTHER INFORMATION: /label= N gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
GGGGCAAATA CAAAA ATG GCT CTT AGC AAG GTC AAA CTA AAT GAC ACT TTC    51
                 Met Ala Leu Ser Lys Val Lys Leu Asn Asp Thr Phe
                   1               5                  10

AAC AAG GAT CAA CTG TTA TCA ACC AGC AAA TAT ACT ATT CAA CGT AGT     99
Asn Lys Asp Gln Leu Leu Ser Thr Ser Lys Tyr Thr Ile Gln Arg Ser
     15                  20                  25

ACA GGT GAC AAC ATT GAT ATA CCC AAT TAT GAT GTA CAA AAA CAT CTC    147
Thr Gly Asp Asn Ile Asp Ile Pr  Asn Tyr Asp Val Gln Lys His Leu
     30                  35                  40
```

```
AAT AAG TTG TGT GGT ATG CTA CTA ATA ACA GAA GAT GCC AAT CAT AAA     195
Asn Lys Leu Cys Gly Met Leu Leu Ile Thr Glu Asp Ala Asn His Lys
 45                 50                  55                  60

TTT ACA GGA TTG ATA GGT ATA TTA TAT GCT ATG TCC CGA TTG GGG AGA     243
Phe Thr Gly Leu Ile Gly Ile Leu Tyr Ala Met Ser Arg Leu Gly Arg
            65                  70                  75

GAA GAT ACC CTT AAA ATA CTC AAA GAT GCA GGC TAC CAA GTA AGG GCC     291
Glu Asp Thr Leu Lys Ile Leu Lys Asp Ala Gly Tyr Gln Val Arg Ala
        80                  85                  90

AAT GGG GTT GAT GTG ATA ACA CAT CGA CAG GAT GTG AAT GGA AAA GAA     339
Asn Gly Val Asp Val Ile Thr His Arg Gln Asp Val Asn Gly Lys Glu
    95                  100                 105

ATG AAA TTT GAA GTG CTA ACA TTA GTC AGC TTA ACA TCA GAA GTT CAA     387
Met Lys Phe Glu Val Leu Thr Leu Val Ser Leu Thr Ser Glu Val Gln
    110                 115                 120

GGC AAT ATA GAA ATA GAG TCA AGG AAG TCT TAC AAA AAG ATG CTA AAA     435
Gly Asn Ile Glu Ile Glu Ser Arg Lys Ser Tyr Lys Lys Met Leu Lys
125                 130                 135                 140

GAG ATG GGA GAG GTA GCC CCA GAA TAC AGA CAT GAC TCT CCT GAT TGT     483
Glu Met Gly Glu Val Ala Pro Glu Tyr Arg His Asp Ser Pro Asp Cys
                145                 150                 155

GGT ATG ATA GTG CTA TGT GTT GCT GCT TTG GTT ATA ACA AAA TTA GCA     531
Gly Met Ile Val Leu Cys Val Ala Ala Leu Val Ile Thr Lys Leu Ala
            160                 165                 170

GCA GGT GAT AGA TCA GGC CTC ACT GCA GTC ATT AGG AGA GCC AAC AAT     579
Ala Gly Asp Arg Ser Gly Leu Thr Ala Val Ile Arg Arg Ala Asn Asn
        175                 180                 185

GTA CTA AGG AAT GAA ATG AAA CAA TAC AAA GGA CTT ATC CCG AAA GAT     627
Val Leu Arg Asn Glu Met Lys Gln Tyr Lys Gly Leu Ile Pro Lys Asp
    190                 195                 200

ATA GCT AAC AGC TTC TAT GAA GTG ATT GAA AAG TAC CCT CAT TAC ATA     675
Ile Ala Asn Ser Phe Tyr Glu Val Ile Glu Lys Tyr Pro His Tyr Ile
205                 210                 215                 220

GAT GTA TTC GTA CAT TTT GGC ATT GCT CAA TCC TCA ACT AGA GGA GGT     723
Asp Val Phe Val His Phe Gly Ile Ala Gln Ser Ser Thr Arg Gly Gly
                225                 230                 235

AGT AGG GTA GAA GGA ATC TTT GCA GGG TTA TTC ATG AAT GCA TAT GGA     771
Ser Arg Val Glu Gly Ile Phe Ala Gly Leu Phe Met Asn Ala Tyr Gly
            240                 245                 250

GCA GGT CAA GTG ATG TTA AGA TGG GGT GTA TTA GCC AAA TCA GTC AAG     819
Ala Gly Gln Val Met Leu Arg Trp Gly Val Leu Ala Lys Ser Val Lys
        255                 260                 265
```

AAC ATT ATG CTT GGT CAT GCC AGC GTG CAA GCA GAA ATG GAA CAG GTT 867
Asn Ile Met Leu Gly His Ala Ser Val Gln Ala Glu Met Glu Gln Val
270 275 280

GTA GAG GTC TAT GAA TAT GCA CAA AAG TTA GGT GGA GAA GCT GGT TTT 915
Val Glu Val Tyr Glu Tyr Ala Gln Lys Leu Gly Gly Glu Ala Gly Phe
285 290 295 300

TAT CAC ATA TTG AAC AAC CCT AAA GCA TCA CTG TTA TCC TTA ACA CAA 963
Tyr His Ile Leu Asn Asn Pro Lys Ala Ser Leu Leu Ser Leu Thr Gln
305 310 315

TTC CCC AAC TTC TCT AGT GTA GTC CTA GGC AAT GCT GCA GGA CTA GGT 1011
Phe Pro Asn Phe Ser Ser Val Val Leu Gly Asn Ala Ala Gly Leu Gly
320 325 330

ATA ATG GGT GAG TAT AGA GGT ACA CCA AGA AAC CAA GAC TTG TAT GAT 1059
Ile Met Gly Glu Tyr Arg Gly Thr Pro Arg Asn Gln Asp Leu Tyr Asp
335 340 345

GCT GCC AAA GCA TAT GCG GAA CAA TTA AAA GAG AAT GGG GTC ATC AAT 1107
Ala Ala Lys Ala Tyr Ala Glu Gln Leu Lys Glu Asn Gly Val Ile Asn
350 355 360

TAC AGT GTA TTA GAT CTG ACT ACA GAG GAA CTA GAG GCA ATC AAG AAC 1155
Tyr Ser Val Leu Asp Leu Thr Thr Glu Glu Leu Glu Ala Ile Lys Asn
365 370 375 380

CAA TTG AAT CCC AAA GAC AAT GAT GTG GAA CTG TGGTATAAA 1197
Gln Leu Asn Pro Lys Asp Asn Asp Val Glu Leu
385 390

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 391 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Met Ala Leu Ser Lys Val Lys Leu Asn Asp Thr Phe Asn Lys Asp Gln
1 5 10 15

Leu Leu Ser Thr Ser Lys Tyr Thr Ile Gln Arg Ser Thr Gly Asp Asn
20 25 30

Ile Asp Ile Pro Asn Tyr Asp Val Gln Lys His Leu Asn Lys Leu Cys
35 40 45

Gly Met Leu Leu Ile Thr Glu Asp Ala Asn His Lys Phe Thr Gly Leu
50 55 60

```
Ile Gly Ile Leu Tyr Ala Met Ser Arg Leu Gly Arg Glu Asp Thr Leu
 65                 70                  75                  80

Lys Ile Leu Lys Asp Ala Gly Tyr Gln Val Arg Ala Asn Gly Val Asp
                85                  90                  95

Val Ile Thr His Arg Gln Asp Val Asn Gly Lys Glu Met Lys Phe Glu
            100                 105                 110

Val Leu Thr Leu Val Ser Leu Thr Ser Glu Val Gln Gly Asn Ile Glu
        115                 120                 125

Ile Glu Ser Arg Lys Ser Tyr Lys Lys Met Leu Lys Glu Met Gly Glu
    130                 135                 140

Val Ala Pro Glu Tyr Arg His Asp Ser Pro Asp Cys Gly Met Ile Val
145                 150                 155                 160

Leu Cys Val Ala Ala Leu Val Ile Thr Lys Leu Ala Ala Gly Asp Arg
                165                 170                 175

Ser Gly Leu Thr Ala Val Ile Arg Arg Ala Asn Asn Val Leu Arg Asn
            180                 185                 190

Glu Met Lys Gln Tyr Lys Gly Leu Ile Pro Lys Asp Ile Ala Asn Ser
        195                 200                 205

Phe Tyr Glu Val Ile Glu Lys Tyr Pro His Tyr Ile Asp Val Phe Val
    210                 215                 220

His Phe Gly Ile Ala Gln Ser Ser Thr Arg Gly Gly Ser Arg Val Glu
225                 230                 235                 240

Gly Ile Phe Ala Gly Leu Phe Met Asn Ala Tyr Gly Ala Gly Gln Val
                245                 250                 255

Met Leu Arg Trp Gly Val Leu Ala Lys Ser Val Lys Asn Ile Met Leu
            260                 265                 270

Gly His Ala Ser Val Gln Ala Glu Met Glu Gln Val Val Glu Val Tyr
        275                 280                 285

Glu Tyr Ala Gln Lys Leu Gly Gly Glu Ala Gly Phe Tyr His Ile Leu
    290                 295                 300

Asn Asn Pro Lys Ala Ser Leu Leu Ser Leu Thr Gln Phe Pro Asn Phe
305                 310                 315                 320

Ser Ser Val Val Leu Gly Asn Ala Ala Gly Leu Gly Ile Met Gly Glu
                325                 330                 335

Tyr Arg Gly Thr Pro Arg Asn Gln Asp Leu Tyr Asp Ala Ala Lys Ala
            340                 345                 350

Tyr Ala Glu Gln Leu Lys Glu Asn Gly Val Ile Asn Tyr Ser Val Leu
        355                 360                 365
```

```
Asp Leu Thr Thr Glu Glu Leu Glu Ala Ile Lys Asn Gln Leu Asn Pr
    370                 375                 380

Lys Asp Asn Asp Val Glu Leu
385                 390
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 949 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 10..777
(D) OTHER INFORMATION: /label= M gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
GGGGCAAAT ATG GAG ACA TAC GTG AAC AAA CTC CAT GAA GGA TCA ATA         48
          Met Glu Thr Tyr Val Asn Lys Leu His Glu Gly Ser Ile
            1               5                  10

TAC ACA GCT GCT GTT CAG TAC AAT GTC ATA GAG AAA GAT GAT GAT CCT       96
Tyr Thr Ala Ala Val Gln Tyr Asn Val Ile Glu Lys Asp Asp Asp Pro
     15                  20                  25

GCA TCT CTC ACA ATA TGG GTT CCC ATG TTC CAA TCA TCC ATC TCT GCC      144
Ala Ser Leu Thr Ile Trp Val Pro Met Phe Gln Ser Ser Ile Ser Ala
 30                  35                  40                  45

GAT ATG CTC ATA AAA GAA CTA ATC AAT GTG AAC ATA TTA GTT CGA CAA      192
Asp Met Leu Ile Lys Glu Leu Ile Asn Val Asn Ile Leu Val Arg Gln
                 50                  55                  60

ATT TCT ACT CCG AAA GGT CCT TCA TTG AAG ATT ATG ATA AAC TCA AGA      240
Ile Ser Thr Pro Lys Gly Pro Ser Leu Lys Ile M t Il  Asn Ser Arg
             65                  70                  75
```

```
AGT GCT GTA CTA GCC CAA ATG CCC AGT AAA TTT ACC ATA AGT GCA AAT      288
Ser Ala Val Leu Ala Gln Met Pro Ser Lys Phe Thr Ile Ser Ala Asn
         80                  85                  90

GTA TCA TTG GAT GAA CGA AGT AAA TTA GCC TAT GAC ATA ACT ACT CCT      336
Val Ser Leu Asp Glu Arg Ser Lys Leu Ala Tyr Asp Ile Thr Thr Pro
     95                 100                 105

TGT GAA ATT AAG GCT TGT AGT TTA ACA TGT TTA AAG GTG AAA AAT ATG      384
Cys Glu Ile Lys Ala Cys Ser Leu Thr Cys Leu Lys Val Lys Asn Met
110                 115                 120                 125

CTC ACT ACT GTG AAA GAT CTC ACC ATG AAA ACA TTC AAT CCT ACC CAT      432
Leu Thr Thr Val Lys Asp Leu Thr Met Lys Thr Phe Asn Pro Thr His
                130                 135                 140

GAG ATC ATT GCA CTG TGT GAA TTT GAA AAT ATC ATG ACA TCC AAA AGA      480
Glu Ile Ile Ala Leu Cys Glu Phe Glu Asn Ile Met Thr Ser Lys Arg
            145                 150                 155

GTT GTT ATA CCA ACT TTC TTA AGG TCA ATC AAT GTA AAA GCA AAG GAT      528
Val Val Ile Pro Thr Phe Leu Arg Ser Ile Asn Val Lys Ala Lys Asp
        160                 165                 170

TTG GAC TCA CTA GAG AAT ATA GCT ACC ACA GAG TTT AAA AAT GCC ATC      576
Leu Asp Ser Leu Glu Asn Ile Ala Thr Thr Glu Phe Lys Asn Ala Ile
    175                 180                 185

ACT AAT GCC AAA ATT ATA CCT TAT GCT GGG TTG GTG TTA GTT ATC ACT      624
Thr Asn Ala Lys Ile Ile Pro Tyr Ala Gly Leu Val Leu Val Ile Thr
190                 195                 200                 205

GTA ACT GAC AAT AAA GGG GCA TTC AAG TAC ATT AAA CCA CAA AGT CAA      672
Val Thr Asp Asn Lys Gly Ala Phe Lys Tyr Ile Lys Pro Gln Ser Gln
                210                 215                 220

TTT ATA GTA GAT CTT GGT GCA TAT CTA GAG AAG GAG AGC ATA TAT TAT      720
Phe Ile Val Asp Leu Gly Ala Tyr Leu Glu Lys Glu Ser Ile Tyr Tyr
            225                 230                 235

GTA ACT ACA AAT TGG AAA CAC ACA GCC ACT AAA TTC TCC ATT AAG CCT      768
Val Thr Thr Asn Trp Lys His Thr Ala Thr Lys Phe Ser Ile Lys Pro
        240                 245                 250

ATA GAG GAC TGATTCTCAC ACAACTTATC TTAACACAAC AGAAGACTCC              817
Ile Glu Asp
    255

CTTGATAACT TACAAATCAT CATGTGATCA AATCCTATTT GCTGCTCTAC CAACCATAAC    877

CATTATATGT TCTCAACCTG ATCAACCCAT CAATTCATCT TGTAGATTAT ACCTCAATTA    937

GATAAATAAA AA                                                        949
```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 256 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Met Glu Thr Tyr Val Asn Lys Leu His Glu Gly Ser Ile Tyr Thr Ala
1 5 10 15

Ala Val Gln Tyr Asn Val Ile Glu Lys Asp Asp Asp Pro Ala Ser Leu
20 25 30

Thr Ile Trp Val Pro Met Phe Gln Ser Ser Ile Ser Ala Asp Met Leu
35 40 45

Ile Lys Glu Leu Ile Asn Val Asn Ile Leu Val Arg Gln Ile Ser Thr
50 55 60

Pro Lys Gly Pro Ser Leu Lys Ile Met Ile Asn Ser Arg Ser Ala Val
65 70 75 80

Leu Ala Gln Met Pro Ser Lys Phe Thr Ile Ser Ala Asn Val Ser Leu
85 90 95

Asp Glu Arg Ser Lys Leu Ala Tyr Asp Ile Thr Thr Pro Cys Glu Ile
100 105 110

Lys Ala Cys Ser Leu Thr Cys Leu Lys Val Lys Asn Met Leu Thr Thr
115 120 125

Val Lys Asp Leu Thr Met Lys Thr Phe Asn Pro Thr His Glu Ile Ile
130 135 140

Ala Leu Cys Glu Phe Glu Asn Ile Met Thr Ser Lys Arg Val Val Ile
145 150 155 160

Pro Thr Phe Leu Arg Ser Ile Asn Val Lys Ala Lys Asp Leu Asp Ser
165 170 175

Leu Glu Asn Ile Ala Thr Thr Glu Phe Lys Asn Ala Ile Thr Asn Ala
180 185 190

Lys Ile Ile Pro Tyr Ala Gly Leu Val Leu Val Ile Thr Val Thr Asp
195 200 205

Asn Lys Gly Ala Phe Lys Tyr Ile Lys Pro Gln Ser Gln Phe Ile Val
210 215 220

Asp Leu Gly Ala Tyr Leu Glu Lys Glu Ser Ile Tyr Tyr Val Thr Thr
225 230 235 240

```
Asn Trp Lys His Thr Ala Thr Lys Phe Ser Ile Lys Pro Ile Glu Asp
                245                 250                 255
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 867 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 18..740
(D) OTHER INFORMATION: /label= P gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

```
GGGGCAAATA CGTCAGT ATG GAA AAA TTT GCA CCT GAG TTT CAT GGA GAA      50
                   Met Glu Lys Phe Ala Pro Glu Phe His Gly Glu
                     1               5                  10

GAT GCC AAT ACA AAA GCA ACC AAG TTT CTT GAA TCC CTA AAA GGA AAA      98
Asp Ala Asn Thr Lys Ala Thr Lys Phe Leu Glu Ser Leu Lys Gly Lys
            15                  20                  25

TTT ACC TCT TCC AAG GAT TCT AGG AAA AAA GAT AGT ATA ATA TCA GTT     146
Phe Thr Ser Ser Lys Asp Ser Arg Lys Lys Asp Ser Ile Ile Ser Val
        30                  35                  40

AAT TCC ATA GAC ATA GAA TTA CCT AAA GAA AGT CCT ATA ACA TCT ACC     194
Asn Ser Ile Asp Ile Glu Leu Pro Lys Glu Ser Pro Ile Thr Ser Thr
    45                  50                  55

AAT CAT AAT ATC AAC CAA CCA AGT GAG ATC AAT GAC ACT ATT GCT GCA     242
Asn His Asn Il  Asn Gln Pro Ser Glu Ile Asn Asp Thr Ile Ala Ala
60                  65                  70                  75

AAT CAA GTT CAT ATC AGA AAG CCT TTG GTA AGC TTC AAA GAA GAA CTG     290
Asn Gln Val His Ile Arg Lys Pro Leu Val Ser Phe Lys Glu Glu Leu
                80                  85                  90
```

```
CCA TCA AGT GAA AAC CCC TTT ACA AAG CTG TAT AAG GAA ACT ATA GAA        338
Pro Ser Ser Glu Asn Pro Phe Thr Lys Leu Tyr Lys Glu Thr Ile Glu
             95                 100                 105

ACA TTT GAC AAT AAT GAA GAA GAA TCA AGC TAC TCA TAT GAT GAG ATA        386
Thr Phe Asp Asn Asn Glu Glu Glu Ser Ser Tyr Ser Tyr Asp Glu Ile
        110                 115                 120

AAT GAT CAA ACA AAT GAT AAT ATA ACA GCA AGA TTA GAT AGG ATA GAT        434
Asn Asp Gln Thr Asn Asp Asn Ile Thr Ala Arg Leu Asp Arg Ile Asp
    125                 130                 135

GAA AAA TTA AGC GAG ATA ATA GGA ATG CTC CAT ACA CTA GTT GTG GCT        482
Glu Lys Leu Ser Glu Ile Ile Gly Met Leu His Thr Leu Val Val Ala
140                 145                 150                 155

AGT GCA GGA CCA ACA GCT GCT CGT GAC GGT ATA AGA GAT GCA ATG GTA        530
Ser Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg Asp Ala Met Val
                160                 165                 170

GGG CTC CGA GAA GAG ATG ATT GAA AAA ATA AGA TCA GAA GCT TTA ATG        578
Gly Leu Arg Glu Glu Met Ile Glu Lys Ile Arg Ser Glu Ala Leu Met
            175                 180                 185

ACT AAC GAT AGA TTA GAA GCA ATG GCC AGG CTT AGG GAT GAA GAG AGT        626
Thr Asn Asp Arg Leu Glu Ala Met Ala Arg Leu Arg Asp Glu Glu Ser
        190                 195                 200

GAA AAG ATG ACA AAA GAT ACA TCA GAT GAA GTA AAA TTA ACC CCT ACC        674
Glu Lys Met Thr Lys Asp Thr Ser Asp Glu Val Lys Leu Thr Pro Thr
    205                 210                 215

TCA GAG AAA CTG AAC ATG GTA TTA GAA GAT GAA AGT AGT GAC AAT GAT        722
Ser Glu Lys Leu Asn Met Val Leu Glu Asp Glu Ser Ser Asp Asn Asp
220                 225                 230                 235

CTA TCA CTT GAA GAT TTC TGAACAGCAA CCAGCACACC AACCAACAGA              770
Leu Ser Leu Glu Asp Phe
                240

TTGGTCAGAT AGAACAACCA TCAATGAGAA AGCCAACCGA TCAGCCAGCC AACCAGTCAC     830

TCAACCAGCC TGTGATTCCA CATAGTTAGT AAAAAAA                              867
```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 241 amino acids
(B) TYPE: amin acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

```
Met Glu Lys Phe Ala Pro Glu Phe His Gly Glu Asp Ala Asn Thr Lys
  1               5                  10                  15

Ala Thr Lys Phe Leu Glu Ser Leu Lys Gly Lys Phe Thr Ser Ser Lys
             20                  25                  30

Asp Ser Arg Lys Lys Asp Ser Ile Ile Ser Val Asn Ser Ile Asp Ile
         35                  40                  45

Glu Leu Pro Lys Glu Ser Pro Ile Thr Ser Thr Asn His Asn Ile Asn
     50                  55                  60

Gln Pro Ser Glu Ile Asn Asp Thr Ile Ala Ala Asn Gln Val His Ile
 65                  70                  75                  80

Arg Lys Pro Leu Val Ser Phe Lys Glu Glu Leu Pro Ser Ser Glu Asn
                 85                  90                  95

Pro Phe Thr Lys Leu Tyr Lys Glu Thr Ile Glu Thr Phe Asp Asn Asn
            100                 105                 110

Glu Glu Glu Ser Ser Tyr Ser Tyr Asp Glu Ile Asn Asp Gln Thr Asn
        115                 120                 125

Asp Asn Ile Thr Ala Arg Leu Asp Arg Ile Asp Glu Lys Leu Ser Glu
    130                 135                 140

Ile Ile Gly Met Leu His Thr Leu Val Val Ala Ser Ala Gly Pro Thr
145                 150                 155                 160

Ala Ala Arg Asp Gly Ile Arg Asp Ala Met Val Gly Leu Arg Glu Glu
                165                 170                 175

Met Ile Glu Lys Ile Arg Ser Glu Ala Leu Met Thr Asn Asp Arg Leu
            180                 185                 190

Glu Ala Met Ala Arg Leu Arg Asp Glu Glu Ser Glu Lys Met Thr Lys
        195                 200                 205

Asp Thr Ser Asp Glu Val Lys Leu Thr Pro Thr Ser Glu Lys Leu Asn
    210                 215                 220

Met Val Leu Glu Asp Glu Ser Ser Asp Asn Asp Leu Ser Leu Glu Asp
225                 230                 235                 240

Phe
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 468 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine resoiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 84..302
(D) OTHER INFORMATION: /label= SH gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

```
TGGGGTAAAT AAAATCTGCA TCCAATCAAG CACAGCACAC ACCGGACACT CCTTGAATCC      60

ACCAGCTGGT TGAACTTATT ACA ATG AAC AAT ACA TCT ACC ATG ATA GAG         110
                          Met Asn Asn Thr Ser Thr Met Ile Glu
                           1               5

TTT ACT GGT AAA TTT TGG ACT TAC TTT ACA TTA GTC TTT ATG ATG TTA       158
Phe Thr Gly Lys Phe Trp Thr Tyr Phe Thr Leu Val Phe Met Met Leu
 10                  15                  20                  25

ATC ATA GGT TTT TTC TTT GTT ATC ACA TCA CTA GTG GCG GCA ATA CTA       206
Ile Ile Gly Phe Phe Phe Val Ile Thr Ser Leu Val Ala Ala Ile Leu
                 30                  35                  40

AAC AAG TTA TGT GAC CTC AAC GAT CAT CAT ACA AAT AGT CTA GAC ATC       254
Asn Lys Leu Cys Asp Leu Asn Asp His His Thr Asn Ser Leu Asp Ile
             45                  50                  55

AGA ACA GGG CTT AGG AAT GAT ACA CAA TCA ATA ACA AGA GCA CAT GTA       302
Arg Thr Gly Leu Arg Asn Asp Thr Gln Ser Ile Thr Arg Ala His Val
         60                  65                  70

TGATCCATCA ACCAATCAAG CAAAAAAGAA GACAACAAAA CAAAAGAAAA TAGCAACATG     362

CATCAAAGTT AAGCAAAGAA AAACCACAAT GGAACAGACA GTCATCACTC ATATCCCTTT     422

AGTCTACAAA TGCTGCATTA TGTACTGTTA ATTAGTTATT TAAAAA                    468
```

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 73 amino acids
(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
Met Asn Asn Thr Ser Thr Met Ile Glu Phe Thr Gly Lys Phe Trp Thr
 1               5                  10                  15

Tyr Phe Thr Leu Val Phe Met Met Leu Ile Ile Gly Phe Phe Phe Val
            20                  25                  30

Ile Thr Ser Leu Val Ala Ala Ile Leu Asn Lys Leu Cys Asp Leu Asn
        35                  40                  45

Asp His His Thr Asn Ser Leu Asp Ile Arg Thr Gly Leu Arg Asn Asp
    50                  55                  60

Thr Gln Ser Ile Thr Arg Ala His Val
 65                  70
```

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 14..1729
(D) OTHER INFORMATION: /label= F gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
GGGGCAAATA AGG ATG GCG ACA ACA ACC ATG AGG ATG ATC ATC AGC ATT        49
               Met Ala Thr Thr Thr Met Arg Met Il  Ile Ser Ile
                1               5                   10

ATC CTC ATC TCT ACC TAT GTG CCA CAT ATC ACT TTA TGC CAG AAC ATA       97
Il  Leu Ile Ser Thr Tyr Val Pro His Ile Thr Leu Cys Gln Asn Ile
        15                  20                  25
```

```
ACA GAA GAA TTT TAT CAA TCG ACA TGC AGT GCA GTT AGT AGA GGT TAC      145
Thr Glu Glu Phe Tyr Gln Ser Thr Cys Ser Ala Val Ser Arg Gly Tyr
     30                  35                  40

CTT AGT GCA TTA AGA ACT GGA TGG TAT ACA AGT GTG GTA ACA ATA GAG      193
Leu Ser Ala Leu Arg Thr Gly Trp Tyr Thr Ser Val Val Thr Ile Glu
 45                  50                  55                  60

TTG AGC AAA ATA CAA AAA AAT GTA TGT AAC GGT ACT GAT TCA AAA GTG      241
Leu Ser Lys Ile Gln Lys Asn Val Cys Asn Gly Thr Asp Ser Lys Val
                 65                  70                  75

AAA TTA ATA AAG CAA GAA CTA GAA AGA TAC AAC AAT GCA GTA GCG GAA      289
Lys Leu Ile Lys Gln Glu Leu Glu Arg Tyr Asn Asn Ala Val Ala Glu
             80                  85                  90

TTG CAA TCA CTT ATG CAA AAT GAA CCG ACC TCC TCT AGT AGA GCA AAA      337
Leu Gln Ser Leu Met Gln Asn Glu Pro Thr Ser Ser Ser Arg Ala Lys
         95                 100                 105

AGA GGG ATA CCA GAG TCG ATA CAT TAT ACA AGA AAC TCT ACA AAA AAG      385
Arg Gly Ile Pro Glu Ser Ile His Tyr Thr Arg Asn Ser Thr Lys Lys
    110                 115                 120

TTT TAT GGA CTA ATG GGC AAA AAG AGA AAA AGG AGA TTT TTA GGA TTC      433
Phe Tyr Gly Leu Met Gly Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe
125                 130                 135                 140

TTG CTA GGT ATT GGA TCT GCT ATT GCA AGT GGT GTA GCA GTG TCC AAA      481
Leu Leu Gly Ile Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys
                145                 150                 155

GTA CTA CAC TTG GAG GGA GAG GTG AAC AAA ATT AAA AAT GCA CTG CTA      529
Val Leu His Leu Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu
            160                 165                 170

TCC ACA AAT AAA GCA GTG GTT AGT CTG TCC AAT GGA GTT AGT GTC CTT      577
Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu
        175                 180                 185

ACT AGC AAA GTA CTT GAT CTA AAG AAC TAT ATA GAC AAA GAG CTT CTA      625
Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr Ile Asp Lys Glu Leu Leu
    190                 195                 200

CCT AAA GTT AAC AAT CAT GAT TGT AGG ATA TCC AAC ATA GCA ACT GTG      673
Pro Lys Val Asn Asn His Asp Cys Arg Ile Ser Asn Ile Ala Thr Val
205                 210                 215                 220

ATA GAA TTC CAA CAA AAA AAC AAT AGA TTG TTG GAA ATT GCT AGG GAA      721
Ile Glu Ph  Gln Gln Lys Asn Asn Arg Leu Leu Glu Ile Ala Arg Glu
                225                 230                 235

TTT AGT GTA AAT GCT GGT ATT ACC ACA CCC CTC AGT ACA TAC ATG TTA      769
Phe Ser Val Asn Ala Gly Il  Thr Thr Pro Leu Ser Thr Tyr Met Leu
            240                 245                 250
```

ACC AAT AGT GAG TTA CTA TCA ATA ATT AAT GAT ATG CCT ATA ACG AAT 817
Thr Asn Ser Glu Leu Leu Ser Ile Ile Asn Asp Met Pro Ile Thr Asn
255 260 265

GAC CAA AAA AAG CTA ATG TCA GTA TGT CAA ATA GTC AGG CAA CAG AGT 865
Asp Gln Lys Lys Leu Met Ser Val Cys Gln Ile Val Arg Gln Gln Ser
270 275 280

TAT TCC ATC ATG TCA GTG TTA AGA GAG GTC ATA GCT TAT GTT GTA CAA 913
Tyr Ser Ile Met Ser Val Leu Arg Glu Val Ile Ala Tyr Val Val Gln
285 290 295 300

TTG CCT CTT TAT GGA GTT ATA GAC ACC CCC TGT TGG AAA CTA CAC ACC 961
Leu Pro Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr
305 310 315

TCT CCA TTA TGC ACC ACT GAT AAT AAA GAA GGG TCA AAC ATC TGC TTA 1009
Ser Pro Leu Cys Thr Thr Asp Asn Lys Glu Gly Ser Asn Ile Cys Leu
320 325 330

ACT AGG ACA GAT CGT GGG TGG TAT TGT GAT AAT GCA GGC TCT GTG TCT 1057
Thr Arg Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser
335 340 345

TTT TTC CCA CAA GCA GAG ACG TGT AAG GTA CAA TCA AAC AGA GTG TTC 1105
Phe Phe Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe
350 355 360

TGT GAC ACA ATG AAC AGT TTA ACT TTG CCT ACT GAT GTT AAC TTA TGC 1153
Cys Asp Thr Met Asn Ser Leu Thr Leu Pro Thr Asp Val Asn Leu Cys
365 370 375 380

AAC ACT GAC ATA TTC AAT TCA AAG TAT GAT TGT AAA ATA ATG ACA TCT 1201
Asn Thr Asp Ile Phe Asn Ser Lys Tyr Asp Cys Lys Ile Met Thr Ser
385 390 395

AAA ACT GAC ATA AGT AGC TCT GTG ATA ACT TCA ATA GGA GCT ATT GTA 1249
Lys Thr Asp Ile Ser Ser Ser Val Ile Thr Ser Ile Gly Ala Ile Val
400 405 410

TCA TGC TAT GGG AAG ACA AAA TGT ACA GCC TCT AAT AAA AAT CGT GGA 1297
Ser Cys Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly
415 420 425

ATC ATA AAG ACT TTT TCC AAT GGG TGT GAT TAT GTA TCA AAC AAA GGA 1345
Ile Ile Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly
430 435 440

GTT GAT ACT GTA TCA GTT GGT AAC ACA CTA TAT TAT GTA AAT AAA CTA 1393
Val Asp Thr Val S r Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Leu
445 450 455 460

GAG GGG AAA GCA CTC TAT ATA AAG GGT GAA CCA ATT ATT AAT TAC TAT 1441
Glu Gly Lys Ala Leu Tyr Ile Lys Gly Glu Pro Ile Ile Asn Tyr Tyr
465 470 475

AAT CCA CTA GTA TTT CCT TCT GAT GAG TTT GAT GCA TCA ATT GCT CAA 1489
Asn Pro Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ala Gln
480 485 490

GTA AAC GCA AAA ATA AAC CAA AGC CTG GCT TTC ATA CGT CGA TCT GAT 1537
Val Asn Ala Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Arg Ser Asp
495 500 505

GAG TTA CTT CAC AGT GTA GAT GTA GGA AAA TCC ACC ACA AAT GTA GTA 1585
Glu Leu Leu His Ser Val Asp Val Gly Lys Ser Thr Thr Asn Val Val
510 515 520

ATT ACT ACT ATT ATC ATA GTG ATA GTT GTA GTG ATA TTA ATG TTA ATA 1633
Ile Thr Thr Ile Ile Ile Val Ile Val Val Val Ile Leu Met Leu Ile
525 530 535 540

ACT GTG GGA TTA CTG TTT TAC TGT AAG ACC AGG AGT ACA CCT ATC ATG 1681
Thr Val Gly Leu Leu Phe Tyr Cys Lys Thr Arg Ser Thr Pro Ile Met
545 550 555

TTA GGG AAG GAT CAG CTT AGT AGT ATC AAC AAT CTT TCC TTT AGT AAA 1729
Leu Gly Lys Asp Gln Leu Ser Ser Ile Asn Asn Leu Ser Phe Ser Lys
560 565 570

TGAAATGCAT AATGTTTACA ATCTTAACCT CAGAATCATA AATGTGATGA GCCAAATTTA 1789

CTGATACATT CAAAAGTTCC ATCTGCCAAG ACCTGCATCT TTATCAGGTC TGCACAAGCT 1849

AACCTTACAT TCTATACTCA GCTCTATGTT AATAGTTATA TAAAA 1894

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 572 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Met Ala Thr Thr Thr Met Arg Met Ile Ile Ser Ile Ile Leu Ile Ser
1 5 10 15

Thr Tyr Val Pro His Ile Thr Leu Cys Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Arg Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr S r Val Val Thr Ile Glu Leu Ser Lys Ile
50 55 60

Gln Lys Asn Val Cys Asn Gly Thr Asp Ser Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Glu Arg Tyr Asn Asn Ala Val Ala Glu Leu Gln Ser Leu
85 90 95

Met Gln Asn Glu Pro Thr Ser Ser Ser Arg Ala Lys Arg Gly Ile Pro
100 105 110

Glu Ser Ile His Tyr Thr Arg Asn Ser Thr Lys Lys Phe Tyr Gly Leu
115 120 125

Met Gly Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Ile
130 135 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Glu Leu Leu Pro Lys Val Asn
195 200 205

Asn His Asp Cys Arg Ile Ser Asn Ile Ala Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Ala Arg Glu Phe Ser Val Asn
225 230 235 240

Ala Gly Ile Thr Thr Pro Leu Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255

Leu Leu Ser Ile Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Val Cys Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met
275 280 285

Ser Val Leu Arg Glu Val Ile Ala Tyr Val Val Gln Leu Pro Leu Tyr
290 295 300

Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys
305 310 315 320

Thr Thr Asp Asn Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp
325 330 335

Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln
340 345 350

Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met
355 360 365

Asn Ser Leu Thr Leu Pro Thr Asp Val Asn Leu Cys Asn Thr Asp Ile
370 375 380

```
Phe Asn Ser Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Il
385                 390                 395                 400

Ser Ser Ser Val Ile Thr Ser Ile Gly Ala Ile Val Ser Cys Tyr Gly
                405                 410                 415

Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr
            420                 425                 430

Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val
        435                 440                 445

Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Leu Glu Gly Lys Ala
    450                 455                 460

Leu Tyr Ile Lys Gly Glu Pro Ile Ile Asn Tyr Tyr Asn Pro Leu Val
465                 470                 475                 480

Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ala Gln Val Asn Ala Lys
                485                 490                 495

Ile Asn Gln Ser Leu Ala Phe Ile Arg Arg Ser Asp Glu Leu Leu His
            500                 505                 510

Ser Val Asp Val Gly Lys Ser Thr Thr Asn Val Val Ile Thr Thr Ile
        515                 520                 525

Ile Ile Val Ile Val Val Val Ile Leu Met Leu Ile Thr Val Gly Leu
    530                 535                 540

Leu Phe Tyr Cys Lys Thr Arg Ser Thr Pro Ile Met Leu Gly Lys Asp
545                 550                 555                 560

Gln Leu Ser Ser Ile Asn Asn Leu Ser Phe Ser Lys
                565                 570
```

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 840 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
- (A) ORGANISM: Bovine r spiratory syncytial virus
- (B) STRAIN: A51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 16..804
(D) OTHER INFORMATION: /label= G gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

```
GGGGCAAATA CAAGC ATG TCC AAC CAC ACC CAT CAT CCT AAA TTC AAG ACA      51
                 Met Ser Asn His Thr His His Pro Lys Phe Lys Thr
                  1               5                  10

TTA AAG AGG GCT TGG AAA GCC TCA AAA TAC TTC ATA GTA GGA TTA TCA       99
Leu Lys Arg Ala Trp Lys Ala Ser Lys Tyr Phe Ile Val Gly Leu Ser
     15                  20                  25

TGT TTA TAT AAG TTC AAT TTA AAG TCC CTT GTC CAA ACG GCT TTG ACC      147
Cys Leu Tyr Lys Phe Asn Leu Lys Ser Leu Val Gln Thr Ala Leu Thr
     30                  35                  40

TCC TTA GCA ATG ATA ACC TTG ACA TCA CTC GTC ATA ACA GCC ATT ATT      195
Ser Leu Ala Met Ile Thr Leu Thr Ser Leu Val Ile Thr Ala Ile Ile
 45                  50                  55                  60

TAC ATT AGT GTG GGA AAT GCT AAA GCC AAG CCC ACA TCC AAA CCA ACC      243
Tyr Ile Ser Val Gly Asn Ala Lys Ala Lys Pro Thr Ser Lys Pro Thr
                 65                  70                  75

ACC CAA CAA ACA CAA CAG CCC CAA AAC CAC ACC CCA CTA CTT CCC ACA      291
Thr Gln Gln Thr Gln Gln Pro Gln Asn His Thr Pro Leu Leu Pro Thr
             80                  85                  90

GAG CAC AAC CAC AAA TCA ACT CAC ACA TCA ACC CAA AGC ACC ACA CTG      339
Glu His Asn His Lys Ser Thr His Thr Ser Thr Gln Ser Thr Thr Leu
         95                 100                 105

TCC CAA CCA CCA AAC ATA GAC ACC ACT AGT GGA ACT ACA TAC GGT CAC      387
Ser Gln Pro Pro Asn Ile Asp Thr Thr Ser Gly Thr Thr Tyr Gly His
    110                 115                 120

CCA ATC AAC AGA ACC CAA AAC AGA AAA ATC AAA AGC CAA TCT ACT CCA      435
Pro Ile Asn Arg Thr Gln Asn Arg Lys Ile Lys Ser Gln Ser Thr Pro
125                 130                 135                 140

CTT GCC ACC CGA AAA CTA CCA ATC AAC CCA CTG GAA AGC AAC CCC CCC      483
Leu Ala Thr Arg Lys Leu Pro Ile Asn Pro Leu Glu Ser Asn Pro Pro
                145                 150                 155

GAA AAC CAC CAA GAC CAC AAC AAC TCC CAA ACA CTC CCT CAT GTG CCC      531
Glu Asn His Gln Asp His Asn Asn Ser Gln Thr Leu Pro His Val Pro
            160                 165                 170

TGC AGC ACA TGC GAA GGC AAT CCT GCC TGT TCA CCA CTC TGC CAA ATC      579
Cys Ser Thr Cys Glu Gly Asn Pro Ala Cys Ser Pro Leu Cys Gln Ile
        175                 180                 185
```

```
GGG CTG GAG AGA GCA CCA AGC AGA GCT CCC ACA ATC ACC CTC AAA AAG     627
Gly Leu Glu Arg Ala Pro Ser Arg Ala Pro Thr Ile Thr Leu Lys Lys
    190                 195                 200

GCT CCA AAA CCC AAA ACC ACC AAA AAA CCA ACC AAG ACA ACA ATC TAC     675
Ala Pro Lys Pro Lys Thr Thr Lys Lys Pro Thr Lys Thr Thr Ile Tyr
205                 210                 215                 220

CAC AGA ACC AGC CCT GAA GCC AAA CTG CAA ACC AAA AAA AAC ACG GCA     723
His Arg Thr Ser Pro Glu Ala Lys Leu Gln Thr Lys Lys Asn Thr Ala
                225                 230                 235

ACT CCA CAA CAA GGC ATC CTC TCT TCA CCA GAA CAC CAA ACA AAT CAA     771
Thr Pro Gln Gln Gly Ile Leu Ser Ser Pro Glu His Gln Thr Asn Gln
            240                 245                 250

TCT ACT ACA CAG ATC TCA CAA CAC ACC TCC ATA TAATATCAAT TATGTTCATA   824
Ser Thr Thr Gln Ile Ser Gln His Thr Ser Ile
        255                 260

TGTAGTTATT TAAAAA                                                   840
```

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 263 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

```
Met Ser Asn His Thr His His Pro Lys Phe Lys Thr Leu Lys Arg Ala
 1               5                  10                  15

Trp Lys Ala Ser Lys Tyr Phe Ile Val Gly Leu Ser Cys Leu Tyr Lys
            20                  25                  30

Phe Asn Leu Lys Ser Leu Val Gln Thr Ala Leu Thr Ser Leu Ala Met
        35                  40                  45

Ile Thr Leu Thr Ser Leu Val Ile Thr Ala Ile Ile Tyr Ile Ser Val
    50                  55                  60

Gly Asn Ala Lys Ala Lys Pro Thr Ser Lys Pro Thr Thr Gln Gln Thr
65                  70                  75                  80

Gln Gln Pro Gln Asn His Thr Pr  Leu Leu Pro Thr Glu His Asn His
                85                  90                  95

Lys Ser Thr His Thr S r Thr Gln S r Thr Thr Leu Ser Gln Pro Pro
            100                 105                 110
```

```
Asn Ile Asp Thr Thr Ser Gly Thr Thr Tyr Gly His Pro Ile Asn Arg
        115                 120                 125

Thr Gln Asn Arg Lys Ile Lys Ser Gln Ser Thr Pro Leu Ala Thr Arg
    130                 135                 140

Lys Leu Pro Ile Asn Pro Leu Glu Ser Asn Pro Pro Glu Asn His Gln
145                 150                 155                 160

Asp His Asn Asn Ser Gln Thr Leu Pro His Val Pro Cys Ser Thr Cys
                165                 170                 175

Glu Gly Asn Pro Ala Cys Ser Pro Leu Cys Gln Ile Gly Leu Glu Arg
            180                 185                 190

Ala Pro Ser Arg Ala Pro Thr Ile Thr Leu Lys Lys Ala Pro Lys Pro
        195                 200                 205

Lys Thr Thr Lys Lys Pro Thr Lys Thr Thr Ile Tyr His Arg Thr Ser
    210                 215                 220

Pro Glu Ala Lys Leu Gln Thr Lys Lys Asn Thr Ala Thr Pro Gln Gln
225                 230                 235                 240

Gly Ile Leu Ser Ser Pro Glu His Gln Thr Asn Gln Ser Thr Thr Gln
                245                 250                 255

Ile Ser Gln His Thr Ser Ile
            260
```

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 961 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: A 51908

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 10..567
(D) OTHER INFORMATION: /label= M2 gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

```
GGGGCAAAT ATG TCA CGA AGA AAT CCC TGC AAA TAT GAG ATT AGG GGA        48
          Met Ser Arg Arg Asn Pro Cys Lys Tyr Glu Ile Arg Gly
            1               5                  10

CAT TGC TTA AAT GGT AAA AAA TGC CAT TTT AGT CAT AAT TAC TTT GAA      96
His Cys Leu Asn Gly Lys Lys Cys His Phe Ser His Asn Tyr Phe Glu
     15                  20                  25

TGG CCT CCA CAT GCT TTA TTA GTG AGG CAA AAT TTT ATG CTA AAT AAG     144
Trp Pro Pro His Ala Leu Leu Val Arg Gln Asn Phe Met Leu Asn Lys
 30                  35                  40                  45

ATA TTA AAA TCT ATG GAC AGG AAC AAC GAT ACC CTG TCA GAA ATA AGT     192
Ile Leu Lys Ser Met Asp Arg Asn Asn Asp Thr Leu Ser Glu Ile Ser
                 50                  55                  60

GGT GCT GCA GAA TTA GAT AGA ACA GAA GAA TAT GCA TTG GGT GTG ATA     240
Gly Ala Ala Glu Leu Asp Arg Thr Glu Glu Tyr Ala Leu Gly Val Ile
             65                  70                  75

GGA GTT TTG GAA AGT TAC TTA AGC TCT ATC AAT AAT ATA ACA AAA CAA     288
Gly Val Leu Glu Ser Tyr Leu Ser Ser Ile Asn Asn Ile Thr Lys Gln
         80                  85                  90

TCA GCC TGT GTT GCT ATG AGT AAA CTA TTA GCC GAG ATT AAC AAT GAT     336
Ser Ala Cys Val Ala Met Ser Lys Leu Leu Ala Glu Ile Asn Asn Asp
     95                 100                 105

GAC ATC AAG AGA TTA AGG AAC AAG GAA GTG CCA ACA TCA CCC AAG ATA     384
Asp Ile Lys Arg Leu Arg Asn Lys Glu Val Pro Thr Ser Pro Lys Ile
110                 115                 120                 125

AGA ATA TAT AAC ACA GTT ATA TCA TAT ATT GAT AGC AAC AAG AGA AAC     432
Arg Ile Tyr Asn Thr Val Ile Ser Tyr Ile Asp Ser Asn Lys Arg Asn
                130                 135                 140

ACA AAA CAA ACT ATA CAT TTG CTT AAG AGA TTG CCT GCA GAC GTG CTT     480
Thr Lys Gln Thr Ile His Leu Leu Lys Arg Leu Pro Ala Asp Val Leu
            145                 150                 155

AAA AAG ACC ATC AAG AAC ACA ATA GAT ATT CAC AAC GAA ATA AAT GGT     528
Lys Lys Thr Ile Lys Asn Thr Ile Asp Ile His Asn Glu Ile Asn Gly
        160                 165                 170

AAT AAC CAA GGT GAC ATA AAT GTT GAT GAA CAA AAT GAA TAACTCCAAC      577
Asn Asn Gln Gly Asp Ile Asn Val Asp Glu Gln Asn Glu
    175                 180                 185

ATTATTATTT TCCCAGAAAA ATACCCCTGT AGCATATCCT CTTTGCTAAT TAAGGATGAA   637

AATGATGTTT TTGTACTAAG TCATCAGAAT GTTCTTGACT GCTTACAGTT TCAATATCCA   697

TATAATATGT ATTCTCAAAA TCATATGCTT GATGATATCT ATTGGACATC ACAGGAGCTG   757
```

ATTGAGGATG TACTTAAGAT TCTTCATCTT TCTGGCATAT CCATAAATAA GTATGTGATA 817

TATGTTTTAG TGCTATAGTA TATAAGTCAC TCAACTATTG ATCAACAGCC ACTTCTTCAT 877

AGCTAGCAAT ATATAAGGAC AAAATGGATA CACTCATTCA TGAGAACTCA ACTAATGTTT 937

ACTTAACAGA TAGTTATTTA AAAA 961

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 186 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

```
Met Ser Arg Arg Asn Pro Cys Lys Tyr Glu Ile Arg Gly His Cys Leu
 1               5                  10                  15

Asn Gly Lys Lys Cys His Phe Ser His Asn Tyr Phe Glu Trp Pro Pro
            20                  25                  30

His Ala Leu Leu Val Arg Gln Asn Phe Met Leu Asn Lys Ile Leu Lys
        35                  40                  45

Ser Met Asp Arg Asn Asn Asp Thr Leu Ser Glu Ile Ser Gly Ala Ala
    50                  55                  60

Glu Leu Asp Arg Thr Glu Glu Tyr Ala Leu Gly Val Ile Gly Val Leu
65                  70                  75                  80

Glu Ser Tyr Leu Ser Ser Ile Asn Asn Ile Thr Lys Gln Ser Ala Cys
                85                  90                  95

Val Ala Met Ser Lys Leu Leu Ala Glu Ile Asn Asn Asp Asp Ile Lys
            100                 105                 110

Arg Leu Arg Asn Lys Glu Val Pro Thr Ser Pro Lys Ile Arg Ile Tyr
        115                 120                 125

Asn Thr Val Ile Ser Tyr Ile Asp Ser Asn Lys Arg Asn Thr Lys Gln
    130                 135                 140

Thr Ile His Leu Leu Lys Arg Leu Pro Ala Asp Val Leu Lys Lys Thr
145                 150                 155                 160

Ile Lys Asn Thr Ile Asp Ile His Asn Glu Ile Asn Gly Asn Asn Gln
                165                 170                 175

Gly Asp Ile Asn Val Asp Glu Gln Asn Glu
            180                 185
```

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 833 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: FS-1

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2..709
(D) OTHER INFORMATION: /label= P gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

GCCTGAGTTT CATGGAGAAG ATGCCAATAC AAAAGCAACC AAGTTTCTTG AATCCCTAAA 60

AGGGAAATTT ACTTCTTCTA AGGATTCTAG GAAAAAAGAT AGTATAATAT CAGTTAATTC 120

CATAGACATA GAATTACCTA AAGAGAGTCC TATAACATCT ACCAATCAAA ATATCAACCA 180

ACTAAGTGAG ATCAATGACA CTATTGCTAC GAATCAAGTT CATATCAGAA AGCCTTTGGT 240

AAGCTTCAAA GAAGAACTGC CATCAAGTGA AAACCCCTTT ACAAGGCTGT ATAAGGAAAC 300

TATAGAAACA TTTGACAATA ATGAAGAAGA ATCAAGCTAC TCATATGATG AGATAAATGA 360

TCAAACAAAT GATAATATAA CAGCAAGACT AGATAGGATA GATGAAAAAT TAAGCGAGAT 420

AATAGGAATG CTCCATACAT TAGTTGTGGC TAGTGCAGGA CCAACAGCTG CTCGTGACGG 480

TATAAGAGAT GCCATGGTAG GGCTCCGAGA AGAGATGATT GAGAAAATAA GATCAGAAGC 540

TTTAATGACT AACGATAGGT TAGAAGCAAT GGCCAGGCTT AGGAATGAAG AGAGTGAAAA 600

GATGAGAAAA GATACATCAG ATGAAGTAAA ATTAACCCCT ACCTCAGAGA AGCTGAACAT 660

GGTATTAGAA GATGAAAGTA GTGACAATGA TCTATCACTT GAAGATTTCT GAATAGCAAC 720

CAGCCCACCC ACCAACAGAT TGGTCAGATA GATCAACCAT CAATGATAAA GCCAACTAAT 780

CAACCAGCCA ACCAGTCACT CAACCAGCCT GTGATTCCAC ATAGTTAGTA AAA 833

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 236 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: FS-1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

```
Pro Glu Phe His Gly Glu Asp Ala Asn Thr Lys Ala Thr Lys Phe Leu
1               5                   10                  15

Glu Ser Leu Lys Gly Lys Phe Thr Ser Ser Lys Asp Ser Arg Lys Lys
            20                  25                  30

Asp Ser Ile Ile Ser Val Asn Ser Ile Asp Ile Glu Leu Pro Lys Glu
        35                  40                  45

Ser Pro Ile Thr Ser Thr Asn Gln Asn Ile Asn Gln Leu Ser Glu Ile
    50                  55                  60

Asn Asp Thr Ile Ala Thr Asn Gln Val His Ile Arg Lys Pro Leu Val
65                  70                  75                  80

Ser Phe Lys Glu Glu Leu Pro Ser Ser Glu Asn Pro Phe Thr Arg Leu
                85                  90                  95

Tyr Lys Glu Thr Ile Glu Thr Phe Asp Asn Asn Glu Glu Glu Ser Ser
            100                 105                 110

Tyr Ser Tyr Asp Glu Ile Asn Asp Gln Thr Asn Asp Asn Ile Thr Ala
        115                 120                 125

Arg Leu Asp Arg Ile Asp Glu Lys Leu Ser Glu Ile Ile Gly Met Leu
    130                 135                 140

His Thr Leu Val Val Ala Ser Ala Gly Pro Thr Ala Ala Arg Asp Gly
145                 150                 155                 160

Ile Arg Asp Ala Met Val Gly Leu Arg Glu Glu Met Ile Glu Lys Ile
                165                 170                 175

Arg Ser Glu Ala Leu Met Thr Asn Asp Arg Leu Glu Ala Met Ala Arg
            180                 185                 190

Leu Arg Asn Glu Glu Ser Glu Lys Met Xaa Lys Asp Thr Ser Asp Glu
        195                 200                 205
```

Val Lys Leu Thr Pro Thr Ser Glu Lys Leu Asn Met Val Leu Glu Asp
    210   215   220

Glu Ser Ser Asp Asn Asp Leu Ser Leu Glu Asp Phe
225   230   235

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1879 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus
(B) STRAIN: FS-1

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 13..1728
(D) OTHER INFORMATION: /label= F gene

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

GGGACAACAG CCATGAGGAT GGTCATCAGC ATTATCTTCA TCTCTACCTA TGTGACACAT 60

ATCACTTTAT GCCAAAACAT AACAGAAGAA TTTTATCAAT CAACATGCAG TGCAGTTAGT 120

AGAGGTTACC TTAGTGCATT AAGAACTGGA TGGTATACAA GTGTGGTAAC AATAGAGTTG 180

AGCAAAATAC AAAAAAATGT GTGTAAAAGT ACTGATTCAA AAGTGAAATT AATAAAGCAA 240

GAACTAGAAA GATACAACAA TGCAGTAATA GAATTGCAGT CACTTATGCA AAATGAACCG 300

GCCTCCTTCA GTAGAGCAAA AAGAGGGATA CCAGAGTTGA TACATTATCC AAGAAACTCT 360

ACAAAAAGGT TTTATGGGCT AATGGGCAAG AAGAGAAAAA GGAGACATTT TAGATTCTTG 420

CTAGGTATTG GATCTGCTAT TGCAAGTGGT GTAGCAGTGT CCAAAGTACT ACACCTGGAG 480

GGAGAGGTGA ATAAAATTAA AAATGCACTG CTATCCACAA ATAAAGCAGT AGTTAGTCTA 540

TCCAATGGAG TTAGTGTCCT TACTAGCAAA GTACTTGATC TAAAGAACTA TATAGACAAA 600

GAGCTTCTAC CTAAAGTTAA CAATCATGAT TGTAGGATAT CCAACATAGG AACTGTGATA 660

GAATTCCAAC AAAAAAACAA TAGATTGTTA GAAATTGCTA GGGAATTTAG TGTAAATGCT 720

GGTATTACCA CACCCCTCAG TACATACATG TTGACCAATA GTGAATTACT ATCACTAATT 780

AATGATATGC CTATAACGAA TGACCAAAAA AAGCTAATGT CAGTATGTCA AATAGTCAGG 840

CAACAGAGTT ATTCCATTAT GTCAGTGTCA AGAGAGGTCA TAGCTTATGA AGTACAATTG 900

CCTATTTATG GAGTTATAGA CACCCCCTGT TGGAAAATAC ACACCTCTCC ATTATGCACC 960

ACTGATAATA AAGAAGGGTC AAACATCTGC TTAACTAGGA CAGATCGTGG GTGGTATTGT 1020

GACAATGCAG GCTCTGTGTC TTTTTTCCCA CAGGCAGAGA CATGTAAGGT ACAATCAAAT 1080

AGAGTGTTCT GTGACACAAT GAACAGTTTA ACTCTGCCTA CTGATGTTAA CTTATGCAAC 1140

ACTGACATAT TCAATACAAA GTATGACTGT AAAATAATGA CATCTAAAAC TGACATAAGT 1200

AGCTCTGTGA TAACTTCAAT TGGAGCTATT GTATCATGCT ATGGGAAGAC AAAATGTACA 1260

GCTTCTAATA AAAATCGTGG AATCATAAAG ACTTTTCCAA TCGGGTGTGA TTATGTATCA 1320

AACAAAGGAG TTGATACTGT ATCTGTTGGT AACACACTAT ATTATGTAAA TAAGCTAGAG 1380

GGGAAAGCAC TCTATATAAA GGGTGAACCA ATTATTAATT ACTATGATCC ATTAGTGTTT 1440

CCTTCTGATG AGTTTGATGC ATCAATTGCC CAAGTAAATG CAAAAATAAA CCAAAGCTTG 1500

GCTTTCATAC GTCGATCTGA TGAGTTACTT CATAGTGTAG ATGTAGGAAA ATCCACCACA 1560

AATGTAGTAA TTACTACTAT TATCATAGTG ATAGTTGTAG TGATATTAAT GTTAATAGCT 1620

GTAGGATTAC TGTTTTACTG TAAGACCAGG AGTACTCCTA TCATGTTAGG GAAGGATCAG 1680

CTTAGTGGTA TCAACAATCT TTCCTTTAGT AAATGAAATG CATAATGTTT ACAATCTAAA 1740

CCTCAGAATC ATAAATGTGA TGAGCTAAAT TTACTAATAC ATTCAAAAGT TCTATCCTCC 1800

AAGACCTGCA TTTTTATCAG GTCTTACATA AGCTAACCTT ACATGCTACA CTCAGCTCCA 1860

TGTTGATAGT TATATAAAA 1879

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 572 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:
(A) ORGANISM: Bovine respiratory syncytial virus

(B) STRAIN: FS-1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

```
Met Gly Thr Thr Ala Met Arg Met Val Ile Ser Ile Ile Phe Ile Ser
1               5                   10                  15

Thr Tyr Val Thr His Ile Thr Leu Cys Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Arg Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Val Thr Ile Glu Leu Ser Lys Ile
    50                  55                  60

Gln Lys Asn Val Cys Lys Ser Thr Asp Ser Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Glu Arg Tyr Asn Asn Ala Val Ile Glu Leu Gln Ser Leu
                85                  90                  95

Met Gln Asn Glu Pro Ala Ser Phe Ser Arg Ala Lys Arg Gly Ile Pro
            100                 105                 110

Glu Leu Ile His Tyr Pro Arg Asn Ser Thr Lys Arg Phe Tyr Gly Leu
        115                 120                 125

Met Gly Lys Lys Arg Lys Arg Arg His Phe Arg Phe Leu Leu Gly Ile
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Glu Leu Leu Pro Lys Val Asn
        195                 200                 205

Asn His Asp Cys Arg Ile Ser Asn Ile Gly Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Ala Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Ile Thr Thr Pro Leu Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu S r Leu Ile Asn Asp Met Pro Il  Thr Asn Asp Gln Lys Lys
            260                 265                 270
```

Leu Met Ser Val Cys Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met
275 280 285

Ser Val Ser Arg Glu Val Ile Ala Tyr Glu Val Gln Leu Pro Ile Tyr
290 295 300

Gly Val Ile Asp Thr Pro Cys Trp Lys Ile His Thr Ser Pro Leu Cys
305 310 315 320

Thr Thr Asp Asn Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp
325 330 335

Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln
340 345 350

Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met
355 360 365

Asn Ser Leu Thr Leu Pro Thr Asp Val Asn Leu Cys Asn Thr Asp Ile
370 375 380

Phe Asn Thr Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Ile
385 390 395 400

Ser Ser Ser Val Ile Thr Ser Ile Gly Ala Ile Val Ser Cys Tyr Gly
405 410 415

Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr
420 425 430

Phe Pro Ile Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val
435 440 445

Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Leu Glu Gly Lys Ala
450 455 460

Leu Tyr Ile Lys Gly Glu Pro Ile Ile Asn Tyr Tyr Asp Pro Leu Val
465 470 475 480

Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ala Gln Val Asn Ala Lys
485 490 495

Ile Asn Gln Ser Leu Ala Phe Ile Arg Arg Ser Asp Glu Leu Leu His
500 505 510

Ser Val Asp Val Gly Lys Ser Thr Thr Asn Val Val Ile Thr Thr Ile
515 520 525

Ile Ile Val Ile Val Val Val Ile Leu Met Leu Ile Ala Val Gly Leu
530 535 540

Leu Phe Tyr Cys Lys Thr Arg Ser Thr Pro Ile Met Leu Gly Lys Asp
545 550 555 560

Gln Leu Ser Gly Ile Asn Asn Leu Ser Phe Ser Lys
565 570

WHAT IS CLAIMED IS:

1. An isolated nucleotide sequence which encodes for a protein of bovine respiratory syncytial virus (BRSV) or a fragment of said nucleotide sequence comprising 15 or more bases wherein said sequence is selected from the group consisting of the nucleocapsid protein gene, the matrix protein gene, the phosphoprotein gene, the small hydrophobic protein gene, the fusion protein gene, the glycoprotein gene and the M2 protein gene.

2. The isolated nucleotide sequence of claim 1 wherein said sequence is a genomic sequence.

3. The isolated nucleotide sequence of claim 2 wherein said sequence is isolated from BRSV strain A51908.

4. The isolated nucleotide sequence of claim 2 wherein said sequence is isolated from BRSV strain FS-1.

5. The isolated nucleotide sequence of claim 2 wherein said sequence is the nucleocapsid protein gene.

6. The isolated nucleotide sequence of claim 5 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:2 or a sequence substantially homologous thereto.

7. The isolated nucleotide sequence of claim 2 wherein said sequence is the matrix protein gene.

8. The isolated nucleotide sequ nc of claim 7 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:4 or a s quence substantially homologous thereto.

9. The isolated nucleotide sequence of claim 2 wherein said sequence is the phosphoprotein gene.

10. The isolated nucleotide sequence of claim 9 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:6 or a sequence substantially homologous thereto.

11. The isolated nucleotide sequence of claim 9 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:16 or a sequence substantially homologous thereto.

12. The isolated nucleotide sequence of claim 2 wherein said sequence is the small hydrophobic protein gene.

13. The isolated nucleotide sequence of claim 12 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:8 or a sequence substantially homologous thereto.

14. The isolated nucleotide sequence of claim 2 wherein said sequence is the fusion protein gene.

15. The isolated nucleotide sequence of claim 14 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:10 or a sequence substantially homologous thereto.

16. The isolated nucleotide sequence of claim 14 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:18 or a sequence substantially homologous thereto.

17. The isolated nucleotide sequence of claim 2 wherein said sequence is the glycoprot in gene.

18. The isolated nucleotide sequence of claim 17 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:12 or a sequence substantially homologous thereto.

19. The isolated nucleotide sequence of claim 2 wherein said sequence is the M2 protein gene.

20. The isolated nucleotide sequence of claim 19 wherein said sequence is defined in the Sequence Listing as SEQ ID NO:14 or a sequence substantially homologous thereto.

21. A replicative cloning vector comprising the nucleotide sequence of claim 6, 8, 10, 11, 13, 15, 16, 18 or 20 and a replicon operative in a host cell.

22. An expression system comprising the nucleotide sequence of claim 6, 8, 10, 11, 13, 15, 16, 18 or 20 operably linked to suitable control sequences.

23. The expression system of claim 22 disposed in a vector capable of replication in suitable host cells.

24. A recombinant host cell transformed with the expression system of claim 22.

25. A method of producing a recombinant BRSV protein selected from the group consisting of nucleocapsid protein, matrix protein, phosphoprotein, small hydrophobic protein, fusion protein, glycoprotein and M2 protein comprising culturing the cells of claim 24 under conditions effective for the production of said BRSV protein.

26. A purified BRSV nucleocapsid protein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:3 or a sequence substantially homologous thereto.

27. A purified BRSV matrix protein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:5 or a sequence substantially homologous thereto.

28. A purified BRSV phosphoprotein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:7 or a sequence substantially homologous thereto.

29. A purified BRSV small hydrophobic protein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:9 or a sequence substantially homologous thereto.

30. A purified BRSV fusion protein or fragment thereof wherein said protein or fragment has the amino acid equence set forth in the Sequence Listing as SEQ ID NO:11 or a sequence substantially homologous thereto.

31. A purified BRSV glycoprotein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:13 or a sequence substantially homologous thereto.

32. A purified BRSV M2 protein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:15 or a sequence substantially homologous thereto.

33. A purified BRSV phosphoprotein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:17 or a sequence substantially homologous thereto.

34. A purified BRSV fusion protein or fragment thereof wherein said protein or fragment has the amino acid sequence set forth in the Sequence Listing as SEQ ID NO:19 or a sequence substantially homologous thereto.

35. An antibody to the BRSV nucleocapsid protein of claim 26.

36. An antibody to the BRSV matrix protein of claim 27.

37. An antibody to the BRSV phosphoprotein of claim 28.

38. An antibody to the BRSV small hydrophobic protein of claim 29.

39. An antibody to the BRSV fusion protein of claim 30.

40. An antibody to the BRSV glycoprotein of claim 31.

41. An antibody to the BRSV M2 protein of claim 32.

42. An antibody to th BRSV phosph protein of claim 33.

43. An antibody to the BRSV fusion protein of claim 34.

44. The antibody of claim 35, 36, 37, 38, 39, 40, 41, 42 or 43 which is a monoclonal antibody.

45. A BRSV vaccine comprising the purified BRSV nucleocapsid protein or fragment thereof of claim 26.

46. A BRSV vaccine comprising the purified BRSV matrix protein or fragment thereof of claim 27.

47. A BRSV vaccine comprising the purified BRSV phosphoprotein or fragment thereof of claim 28.

48. A BRSV vaccine comprising the purified BRSV small hydrophobic protein or fragment thereof of claim 29.

49. A BRSV vaccine comprising the purified BRSV fusion protein or fragment thereof of claim 30.

50. A BRSV vaccine comprising the purified BRSV glycoprotein or fragment thereof of claim 31.

51. A BRSV vaccine comprising the purified BRSV M2 protein or fragment thereof of claim 32.

52. A BRSV vaccine comprising the purified BRSV phosphoprotein or fragment thereof of claim 33.

53. A BRSV vaccine comprising the purified BRSV fusion protein or fragment thereof of claim 34.

54. A method of detecting BRSV infection using a probe comprising the isolat d nucleotide sequence of claim 6, 8, 10, 11, 13, 15, 16, 18 or 20.

55. A method of detecting antibodies to BRSV using the purified BRSV nucleocapsid protein or fragment thereof of claim 26.

56. A method of detecting antibodies to BRSV using the purified BRSV matrix protein or fragment thereof of claim 27.

57. A method of detecting antibodies to BRSV using the purified BRSV phosphoprotein or fragment thereof of claim 28.

58. A method of detecting antibodies to BRSV using the purified BRSV small hydrophobic protein or fragment thereof of claim 29.

59. A method of detecting antibodies to BRSV using the purified BRSV fusion protein or fragment thereof of claim 30.

60. A method of detecting antibodies to BRSV using the purified BRSV glycoprotein or fragment thereof of claim 31.

61. A method of detecting antibodies to BRSV using the purified BRSV M2 protein or fragment thereof of claim 32.

62. A method of detecting antibodies to BRSV using the purified BRSV phosphoprotein or fragment thereof of claim 33.

63. A method of detecting antibodies to BRSV using the purified BRSV fusion protein or fragment thereof of claim 34.

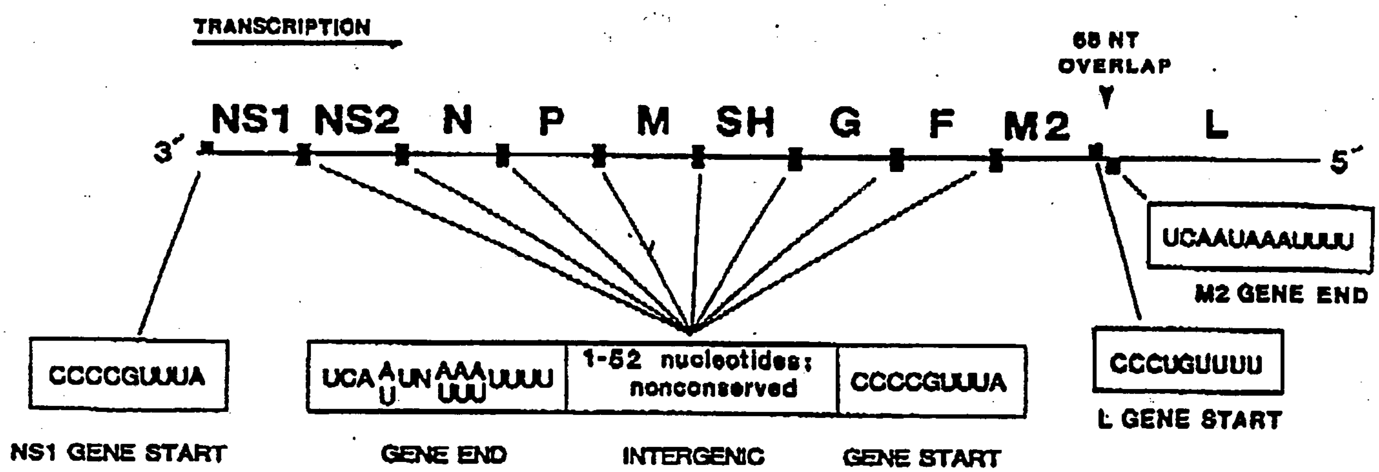
TRANSCRIPTION
68 NT
OVERLAP
3'
NS1 NS2 N P M SH G F M2 L
5'
UCAAUAAAUUUU
M2 GENE END
CCCCGUUUA
NS1 GENE START
UCA A U UN AAA UUU UUUU
GENE END
1-52 nucleotides; nonconserved
INTERGENIC
CCCCGUUUA
GENE START
CCCUGUUUU
L GENE START

FIG. 1

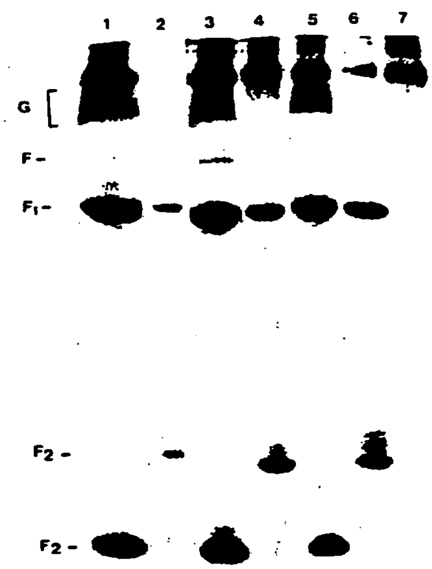

FIG. 2

Cross-immunoprecipitation of [^{3}H] glucosamine labeled antigens using BRSV aniserum: [^{3}H] glucosamine labeled antigens were immunoprecipitated using BRSV (A51908) antiserum. The immunoprecipates were analyzed on a 12.5% SDS-PAGE. Lane 1: GRSV, lane 2: HRSV, lane 3: FS-1 (BRSV), lane 4: A51908 (BRSV), lane 5: VC-464 (BRSV), and lane 6: Md-x (BRSV), and lane 7: uninfected control.

3/3

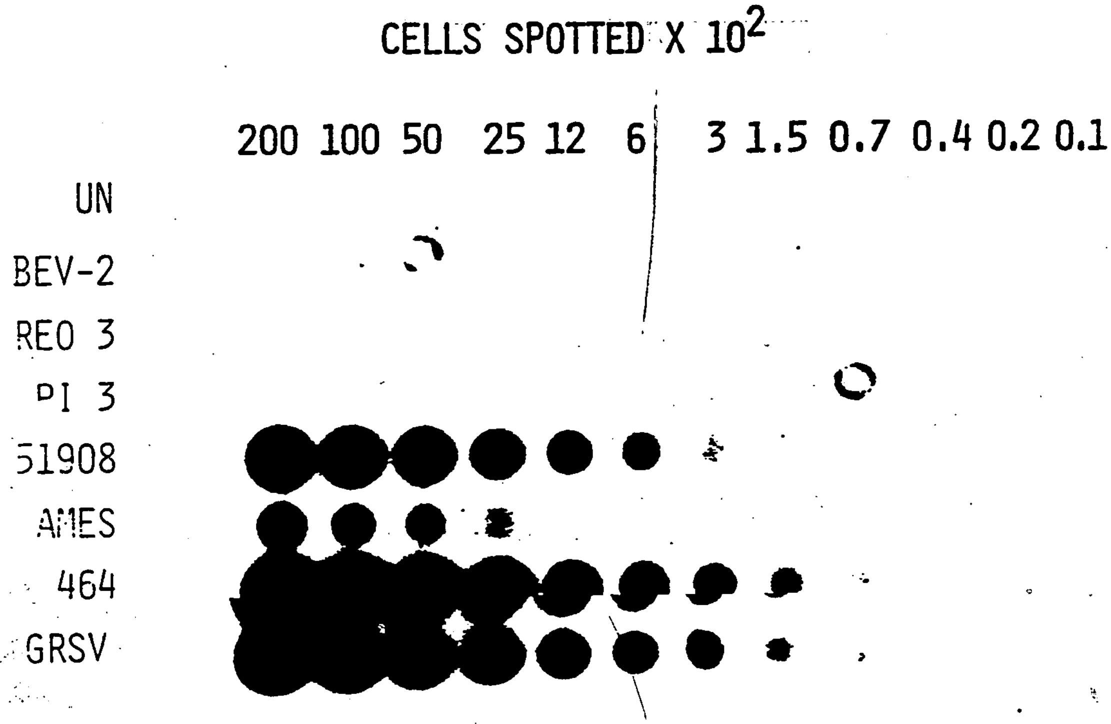

FIG. 3

Autoradiograph of the hybridization of ^{32}P-labeled BRSV-N gene probe to the RNA of different bovine respiratory viruses.